Hypertension Research (2021) 44:1205–1212
https://doi.org/10.1038/s41440-021-00681-7

ARTICLE

# Isometric handgrip exercise training reduces resting systolic blood pressure but does not interfere with diastolic blood pressure and heart rate variability in hypertensive subjects: a systematic review and meta-analysis of randomized clinical trials

João Pedro Arantes de Sousa Almeida[1] · Murilo Bessa[1] · Leandro Teixeira Paranhos Lopes[2] · Alexandre Gonçalves[1] · Leonardo Roever[3] · Hugo Ribeiro Zanetti[4,5]

Received: 25 January 2021 / Revised: 6 April 2021 / Accepted: 14 May 2021 / Published online: 17 June 2021


**Abstract**

To evaluate the effects of isometric handgrip exercise training (IHET) on blood pressure and heart rate variability in hypertensive subjects. Five databases were searched for randomized clinical trials in English, Spanish, or Portuguese evaluating the effect of IHET vs. no exercise on blood pressure (systolic and/or diastolic) and/or heart rate variability (low frequency [LF], high frequency [HF], and/or LF/HF ratio) through December 2020. Random-effects meta-analyses of mean differences (MDs) and/or standardized mean differences (SMDs) with 95% confidence intervals (CIs) were performed. Five trials were selected ($n = 324$ hypertensive subjects), whose durations ranged from 8 to 10 weeks. Compared to no exercise, IHET reduced systolic blood pressure (MD −8.11 mmHg, 95% CI −11.7 to −4.53, $p < 0.001$) but did not affect diastolic blood pressure (MD −2.75 mmHg, 95% CI −9.47–3.96, $p = 0.42$), LF (SMD −0.14, 95% CI −0.65–0.37, $p = 0.59$), HF (SMD 0.38, 95% CI −0.14–0.89, $p = 0.15$), or the LF/HF ratio (SMD −0.22, 95% CI −0.95–0.52, $p = 0.57$). IHET performed for 8–10 weeks had a positive effect on resting systolic blood pressure but did not interfere with diastolic blood pressure or heart rate variability in hypertensive subjects. These data should be interpreted with caution since all volunteers included in the studies were clinically medicated and their blood pressure was controlled.

**Keywords** Isometric exercise · Hypertension · Blood pressure · Heart rate variability

## Introduction

Cardiovascular diseases remain the major cause of death and morbimortality worldwide. The prevalence has doubled since 1990, affecting 523 million people and causing 18.6 million deaths in 2019 [1]. There are multiple traditional risk factors for developing cardiovascular diseases, including cardiometabolic, behavioral, environmental, and social issues [2].

Hypertension remains the first modifiable risk factor for cardiovascular disease and plays a key role in cardiovascular outcomes, such as myocardial infarction, stroke, and heart failure [1]. Furthermore, hypertension can lead to autonomic imbalance assessed by heart rate variability (HRV), which is associated with immune dysfunction, chronic inflammation, and all-cause mortality [3–5]. Interventions become necessary to reverse these conditions.

Exercise training has been deemed an additional, nonpharmacological tool to treat hypertension. Traditionally, moderate aerobic exercise is the most recommended type of exercise for hypertensive subjects, as it reduces resting blood pressure by 8.9 mmHg [6]. However, recent studies have shown that dynamic resistance training can reduce

✉ Hugo Ribeiro Zanetti
hugo.zanetti@hotmail.com

1 Department of Medicine, IMEPAC University Center, Araguari, MG, Brazil

2 Department of Medicine, Brazil University, Fernandópolis, SP, Brazil

3 Department of Clinical Research, Federal University of Uberlândia, Uberlândia, MG, Brazil

4 Department of Physical Education and Department of Medicine, IMEPAC University Center, Araguari, MG, Brazil

5 PostGraduate Program in Physical Education, Federal University of Triângulo Mineiro, Uberaba, MG, Brazil

resting blood pressure as much as or more than aerobic exercise [7–9]. Although the benefits of both aerobic and resistance training are unquestionable for hypertension treatment, personal, social, and economic factors can lead to low adherence and withdrawal of exercise programs, thus interrupting their benefits.

Isometric handgrip exercise training (IHET) has been proposed as a low-cost intervention with superior adherence compared to other exercise modalities [10, 11]. This type of exercise involves sustained contraction against an immovable load or resistance with minimal or no change in length of the muscle group involved [12]. The main concern over IHET in hypertensive subjects has been the prolonged cardiovascular response during muscle contractions, but recent studies have demonstrated safe blood pressure values during stress [13].

Previous studies have evaluated the effect of IHET on resting blood pressure and have shown significant reductions in systolic blood pressure (SBP) and diastolic blood pressure (DBP) without any effect on HRV in normotensive individuals [14, 15]. However, studies involving hypertensive subjects remain scarce. Thus, this systematic review and meta-analysis aimed to evaluate the effects of IHET on resting blood pressure and HRV in hypertensive subjects compared to no-exercise groups in randomized controlled trials. We hypothesized that IHET would reduce resting blood pressure but would not interfere with HRV.

# Methods

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines [16] and was registered in the PROSPERO database (CRD42020219089).

## Eligibility criteria

We included randomized clinical trials that compared a group performing IHET with an exercise training protocol duration of at least 4 weeks against a nonexercise group (control group) and evaluated the resting blood pressure (systolic and/or diastolic) and/or HRV of treated hypertensive adults (over 18 years old) using frequency-domain parameters derived from the spectral analysis of heart rate, high frequency (HF), low frequency (LF), and HF/LF ratio. We excluded studies that involved normotensive or untreated hypertensive adults, evaluated the effect of two or more exercise modalities/interventions, evaluated the acute effect of IHET, and did not report the pre to postintervention or delta score in blood pressure or HRV.

## Search strategy

We searched the PubMed, Europe PMC, Cochrane, Web of Science, Scielo, and SPORTDiscuss databases without language restrictions up to December 2020. We also searched for unpublished or ongoing trials using the System for Information on Gray Literature in Europe. We used the following terms: isometric handgrip AND exercise AND blood pressure AND HRV AND hypertension AND adults.

## Study selection

Initially, two reviewers (LTPL and HR) independently screened the titles, abstracts, and, when necessary, the full texts from database records according to the eligibility criteria. Duplicates and articles that did not meet the criteria were removed. In the event of a disagreement between the two reviewers, a third reviewer was included. The reviewers were not blinded to the names or institutions of study authors or to journal titles.

## Data extraction

The data extraction for all variables was performed by two independent researchers (JPASA and MB) using a customized Excel® spreadsheet. Then, the data were checked, and a third researcher was consulted in case of disagreement. The data extracted from the articles were as follows: (1) study details (i.e., year of publication, country of research); (2) number of initial participants involved in the study; (3) number of participants who finished the intervention; (4) training protocol; and (5) outcomes. Quantitative data from pre and posttraining interventions were extracted from the text, tables, and figures of articles and computed as the mean ± standard deviation (SD). When the results were presented as the standard error of the mean, the standard error was converted to the SD.

## Risk of bias and quality of evidence assessment

Two researchers (AL and LR) assessed the quality of the included studies using the Cochrane Collaboration tool for risk of bias [17]. The Grading of Recommendations Assessment Development and Evaluation (GRADE) tool was used to assess the quality of evidence per outcome, and each article was graded from high quality to very low quality [18].

## Statistical analysis

We used a random-effects model for meta-analysis. For all studies, the delta (post-pre) values were calculated for outcomes, and the SD change was calculated according to

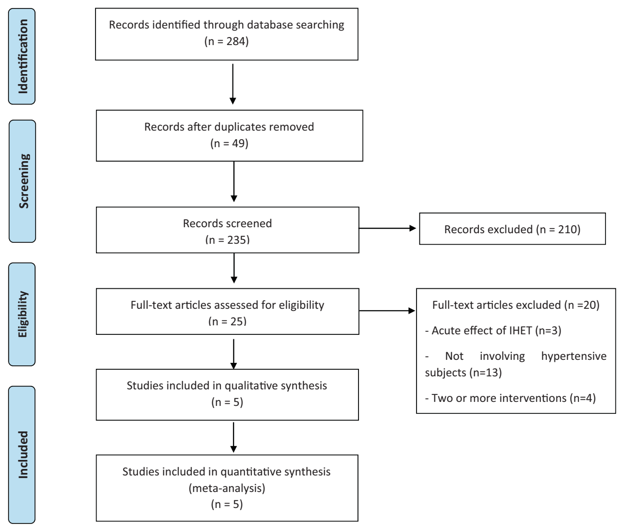


**Fig. 1** Flow diagram of the study selection process

the equation $SD\,change = \sqrt{[(SDpre)^2 + (SDpost)^2 - (2 \times corr \times SDpre \times SDpost)]}$, where the imputed correlation coefficient was 0.5 [19]. Effects on blood pressure are presented as the mean differences, and HRV is presented as the standard mean difference (SMD), with 95% confidence intervals (CIs). Cochran's Q-statistic and $I^2$ test were performed to test for heterogeneity between studies. The heterogeneity thresholds for $I^2$ were 25% (low), 50% (moderate), and 75% (high) [20]. Furthermore, the mean effect size was estimated by Hedges' *g* test. Meta-analyses were performed using Review Manager 5.3 for Windows.

## Results

We searched the PubMed, Europe PMC, Cochrane, Web of Science, Scielo, and SPORTDiscuss databases and

**Table 1** Summary of included studies

| Author (country) | Initial no. of participants (M/F) | Final no. of participants | Age of participants | Pre resting blood pressure (mmHg) | | Exercise frequency and duration of study | IHET training | Outcomes |
|---|---|---|---|---|---|---|---|---|
| | | | | Systolic | Diastolic | | | |
| Stiller-Moldovan (Canada) [24] | TG: 8/5<br>CG: 6/7 | TG: 7/4<br>CG: 3/6 | TG: 60.0 ± 8.5<br>CG: 62.7 ± 6.1 | TG: 113.9 ± 12.7<br>CG: 117.8 ± 14.3 | TG: 60.7 ± 11.6<br>CG: 67.5 ± 4.2 | 3×/week for 8 weeks. | 4 × 2 min bilateral IHET contractions at 30–40% MVC, separated by 1-min rest | ↔ SBP<br>↔ DBP<br>↔ LF<br>↔ HF<br>↔ LF/HF |
| Badrov (Canada) [21] | TG: 6/6<br>CG: 7/5 | TG: 6/6<br>CG: 7/5 | TG: 65 ± 7<br>CG: 63 ± 9 | TG: 129 ± 16<br>CG: 130 ± 17 | TG: 72 ± 9<br>CG: 73 ± 12 | 3×/week for 8 weeks | 4 × 2 min unilateral (non-dom) IHET contractions at 30%MVC separated by 4-min rest | ↓ SBP<br>↓ DBP |
| Taylor (Canada) [25] | TG: 5/4<br>CG: 5/3 | TG: 5/4<br>CG: 5/3 | TG: 69.3 ± 6.0<br>CG: 64.2 ± 5.5 | TG: 156.0 ± 9.4<br>CG: 152.0 ± 7.8 | TG: 82.3 ± 9.3<br>CG: 87.1 ± 10.8 | 3×/week for 10 weeks | 4 × 2 min bilateral IHET contractions at 30% MVC, separated by 1-min rest | ↓ SBP<br>↔ DBP<br>↔ LF<br>↑ HF<br>↔ LF/HF |
| Millar (Canada) [22] | TG: 11/2<br>CG: 7/3 | TG: 11/2<br>CG: 7/3 | TG: 65 ± 6<br>CG: 67 ± 6 | TG: 125 ± 12<br>CG: 128 ± 16 | TG: 78 ± 2<br>CG: 75 ± 8 | 3×/week for 8 weeks | 4 × 2 min unilateral IHET contractions at 30% MVC, separated by 4-min rest | ↓ SBP<br>↔ DBP<br>↔ LF<br>↔ HF<br>↓ LF/HF |
| Punia (India) [23] | Total of 40 participants | Total of 40 participants | Between 30 and 45 years | TG: 144.15 ± 7.63<br>CG: 142.40 ± 7.54 | TG: 92.65 ± 4.90<br>CG: 89.50 ± 4.60 | 3×/week for 8 weeks | 4 × 2 min unilateral at 30% MVC separated by 4-min rest. | ↓ SBP<br>↓ DBP |

*TG* training group, *CG* control group, *MVC* maximum voluntary contraction, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *LF* low frequency, *HF* high frequency, *LF/HF* low-frequency/high-frequency ratio

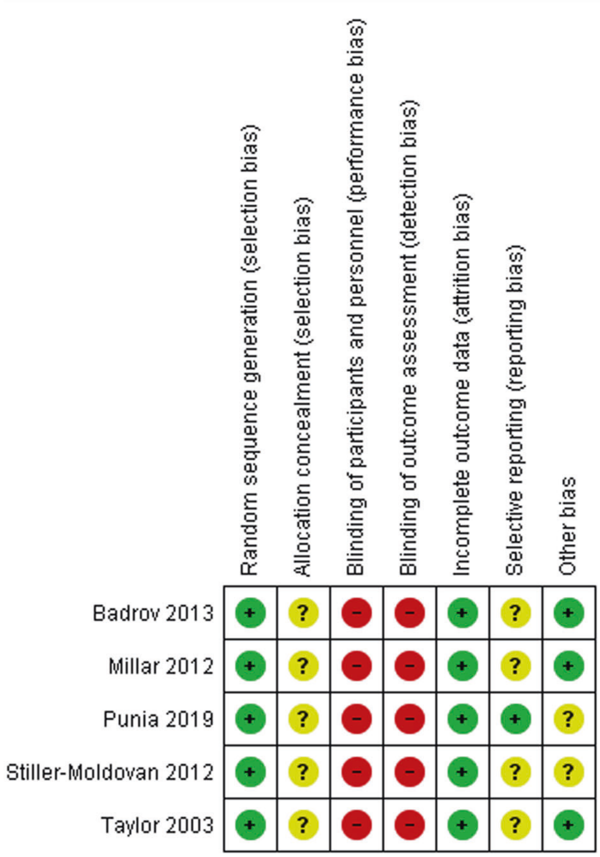


**Fig. 2** Risk of bias summary: review authors' judgments about each risk-of-bias item for each included study

found 284 records. No additional records from other sources were found. From the total, 49 duplicates were removed, leaving 235 records. After screening titles and abstracts, 210 articles were excluded. The remaining 25 articles were read in full, and 20 were excluded. Therefore, five articles were included in the present study. Figure 1 shows a flow diagram.

Table 1 presents the details of the included studies: the age of the participants, prestudy resting blood pressure values, exercise training protocols, and main findings. A total of 330 volunteers were initially included, and 324 completed the study, representing a sample loss of 1.13%.

## Risk of bias

We evaluated the risk of bias using the Cochrane Collaboration tool. Figure 2 shows the results. In our judgment, all included studies had a high risk of bias for not discussing the blinding of participants and personnel and the blinding of outcome assessment [21–25]. Furthermore, we deemed the following unclear: allocation concealment for all studies [21–25], selective reporting for four studies [21, 22, 24, 25], and other bias for three studies [23, 24].

## Quality of evidence

We used GRADE to assess the quality of evidence. Table 2 shows the results. We found moderate evidence for SBP, DBP, HF, LF, and HF/LF. The (−1) downgrade was due to the lack of blinding information on study participants.

## Meta-analyses

### Blood pressure

All five included articles evaluated the effect of intervention with IHET on SBP and DBP [21–25]. As Fig. 3a illustrates, SBP was significantly reduced (MD −8.11 mmHg, 95% CI –11.7 to −4.53, $p < 0.0001$, $I^2 = 0\%$). However, no difference was observed in DBP (MD −2.75 mmHg, 95% CI −9.47–3.96, $p = 0.42$, $I^2 = 80\%$), as shown in Fig. 3b.

### Heart rate variability

Three studies evaluated the effect of IHET on HF, LF, and the HF/LF ratio [22, 24, 25]. There was no significant difference in HF (SMD 0.38, 95% CI −0.14–0.89, $p = 0.15$, $I^2 = 0\%$) (Fig. 4a), LF (SMD −0.14, 95% CI −0.65–0.37, $p = 0.59$, $I^2 = 0\%$) (Fig. 4b), or HF/LF (SMD −0.22, 95% CI −0.95–0.52, $p = 0.57$, $I^2 = 49\%$) (Fig. 4c).

## Discussion

Our study aimed to evaluate the effects of IHET on blood pressure and HRV in hypertensive subjects. We found a significant reduction in SBP with no effect on DBP or HRV. We can infer, then, that interventions using IHET are beneficial for treating hypertensive subjects. However, these data should be interpreted with caution since all volunteers included in the studies were clinically medicated and their blood pressure was properly controlled.

Our findings showed that IHET reduced SBP (mean 8.11 mmHg) but not DBP. These data are clinically relevant, as reduced SBP is associated with lower mortality from coronary heart disease, stroke, and other causes [26]. A previous study found similar reductions in SBP regardless of subject classification (normotensive, prehypertensive, hypertensive), but greater reductions were observed in prehypertensive populations [14]. Although the precise mechanisms that reduce SBP when using IHET have remained controversial, the explanation has focused on the reduction in systemic vascular resistance. This phenomenon could be explained by both the increase in endothelial-dependent vasodilation in response to reactive hyperemia—caused by isometric muscle contraction—and shear stress, which heightens the bioavailability of nitric oxide

**Table 2** Quality of evidence using GRADE tool

| Certainty assessment | | | | | | | Summary of findings | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Participants (studies) Follow up | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | Overall certainty of evidence | Study event rates (%) | | Anticipated absolute effects | |
| | | | | | | | Control | IHET | Risk with control | Risk difference with IHET |
| Systolic blood pressure | | | | | | | | | | |
| 324 (5 RCTs) | Serious[a] | Not serious | Not serious | Not serious | Publication bias strongly suspected strong association[a] | ⨁⨁⨁◯ MODERATE | 259 | 265 | The mean SBP was 0.23 mmHg | MD 8.11 mmHg lower (11.70 lower to 4.53 lower) |
| Diastolic blood pressure | | | | | | | | | | |
| 324 (5 RCTs) | Serious[a] | Not serious | Not serious | Not serious | Publication bias strongly suspected strong association[a] | ⨁⨁⨁◯ MODERATE | 259 | 265 | The mean DBP was 1.25 mmHg | MD 2.75 mmHg lower (9.47 lower to 3.96 higher) |
| HF | | | | | | | | | | |
| 60 (3 RCTs) | Serious[a] | Not serious | Not serious | Not serious | Publication bias strongly suspected strong association[a] | ⨁⨁⨁◯ MODERATE | 27 | 33 | – | SMD **0.38 higher** (0.14 lower to 0.89 higher) |
| LF | | | | | | | | | | |
| 60 (3 RCTs) | Serious[a] | Not serious | Not serious | Not serious | Publication bias strongly suspected strong association[a] | ⨁⨁⨁◯ MODERATE | 27 | 33 | – | SMD **0.14 lower** (0.65 lower to 0.37 higher) |
| LF/HF | | | | | | | | | | |
| 60 (3 RCTs) | Serious[a] | Not serious | Not serious | Not Serious | Publication bias strongly suspected strong association[a] | ⨁⨁⨁◯ MODERATE | 27 | 33 | – | SMD **0.22 lower** (0.95 lower to 0.52 higher) |

*CI* confidence interval, *SMD* standardized mean difference

[a](-1) lack of blinding information on study participants

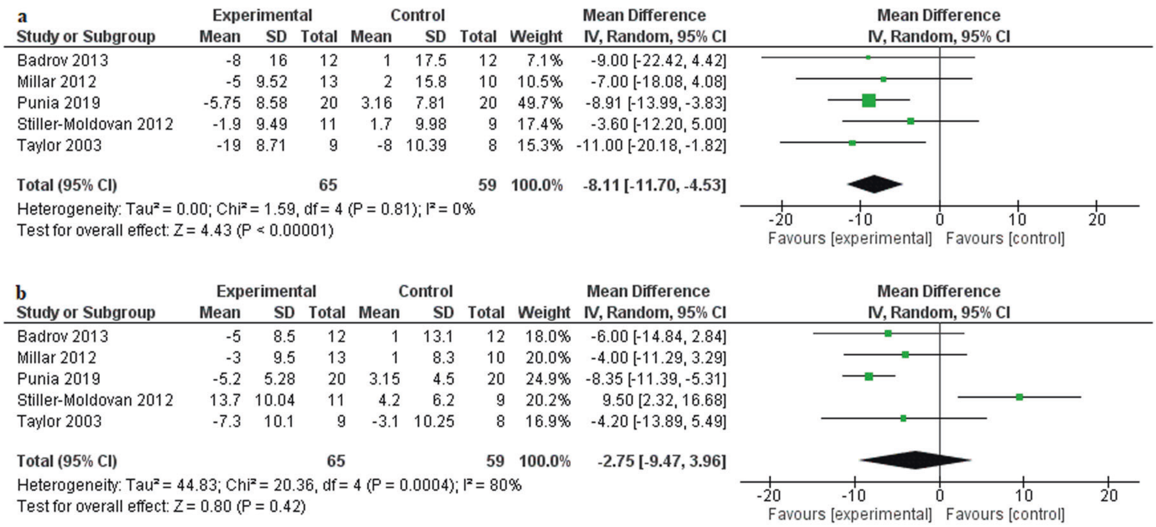


**Fig. 3** Forest plot comparing the IHET group vs. the control group on **a** SBP and **b** DBP

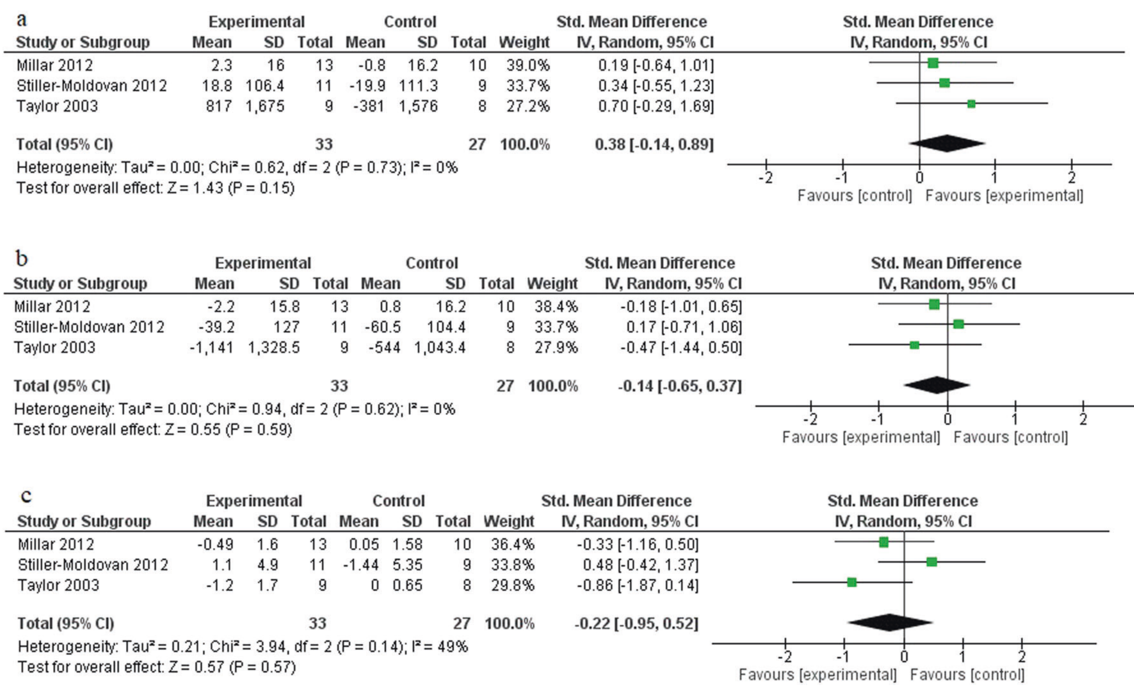


**Fig. 4** Forest plot comparing the IHET group vs. the control group on **a** HF, **b** LF, and **c** the HF/LF ratio

[8, 27–29]. Furthermore, one-leg isometric exercise training increased vessel endothelial function, artery diameter of trained limb, blood velocity, and blood flow and reduced vascular conductance [30]. Other factors, such as improved oxidative stress markers, reduced sympathetic activity, and ischemia-reperfusion processes, can explain this phenomenon [31–33]. Most volunteers had normalized DBP values at the beginning of the training due to the use of anti-hypertensive drugs with peripheral actions (i.e., angiotensin-converting enzyme inhibitors, aldosterone antagonists, and diuretics). This could possibly explain why exercise had little influence on DBP.

Although all studies included in this meta-analysis were carried out with medicated individuals, two studies included volunteers with resting SBP above 140 mmHg. Based on the principle that a reduction in blood pressure is magnified in individuals with a higher resting blood pressure before the period of physical training, attention is warranted when interpreting the data from our study [34, 35]. We emphasize that all volunteers were clinically medicated, demonstrating that IHET could be a useful tool for improving resting blood pressure.

Acute and chronic factors may influence the blood pressure response immediately after physical exercise and at rest. Stress time (time of isometric contraction) is important for postexercise hypotension: the longer the stimulus time is, the higher the hypertensive peak will be—producing higher postexercise reactive hypotension. Thus, repeated physical training sessions can lead to chronic blood pressure adjustments [36]. The intensity of isometric contractions should also be considered. All five included studies performed IHET at 30% of maximum voluntary contration MVC. One study showed that IHET performed at different intensities (30% vs. 50% MVC) did not acutely promote cardiac overload and did not potentiate postexercise hypotension in this population. However, the protocol stress time in each bout was short (10 s), which could interfere with the analysis of results [13]. The intensity of exercise should be a considerable factor when the stress duration is longer; a higher intensity promotes higher postexercise hypotension [37]. We encourage new studies to evaluate and stabilize the ideal intensity zone of IHET that promotes the best hypotensive response.

As mentioned, when prescribing isometric exercises with prolonged stress time, one concern is that the longer the stress time is, the greater the hypertensive peak during exercise will be—and this is enhanced if a large muscle group is involved [38, 39]. Therefore, despite the need for further studies, we believe that since IHET uses a small muscle group, the hypertensive peak during stress is lower, making this type of exercise a viable and safe alternative.

Hypertensive subjects have autonomic dysfunction, with a lower HF domain and a larger LF and LF/HF domain. Low levels of HRV are associated with cardiac events, such as heart disease, heart failure, diabetes, and myocardial infarction [40–42]. Our results corroborate other studies that found no effect of resistance training on HRV [43–46]. However, a recent study suggested that aerobic exercise training has a positive effect on HRV, which could be explained by plasma catecholamine levels, nitric oxide levels, and neuromodulation [47, 48]. We believe that exercise training variables (frequency, intensity, and type of exercise) and time of intervention could interfere with HRV modulation. New studies with these variable manipulations using IHET are needed.

Our study has limitations. The small number of studies conducted with hypertensive people can directly influence the results found. Therefore, we encourage further research on IHET in this population using different intensities, contraction times, and intervention times. In addition, three studies evaluated the effect of IHET on HRV—possibly impairing the real analysis of the effect of physical exercise.

We encourage new studies to evaluate the effectiveness of IHET in hypertensive subjects using different intensities, stress times, types of execution, weekly frequencies, and intervention lengths. Such future studies can help define the ideal dose-response of hypertensive subjects to IHET.

## Conclusion

We conclude that IHET performed for 8–10 weeks has a positive effect on SBP but no effect on DBP or HRV in hypertensive subjects.

### Compliance with ethical standards

**Conflict of interest** The authors declare no competing interests.

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