Effects of dynamic, isometric, and combined resistance training on ambulatory blood pressure in treated men with hypertension: a randomized controlled trial

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Conflicts of interest

None

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ABSTRACT

Ambulatory blood pressure (ABP) monitoring is a widespread recommendation for the diagnosis and management of hypertension. Dynamic resistance training (DRT) and isometric handgrip training (IHT) have been recommended for hypertension treatment, but their effects on ABP have been poorly studied. Additionally, combined dynamic and isometric handgrip resistance training (CRT) could produce an additive effect that has yet to be tested. Thus, this randomized controlled trial was designed to evaluate the effects of DRT, IHT and CRT on mean ABP and ABP variability**.** Fifty-nine treated men with hypertension were randomly allocated to 1 of four groups: DRT (8 dynamic resistance exercises, 50% of 1RM, 3 sets until moderate fatigue), IHT (4 sets of 2 min of isometric handgrip at 30% of MVC), CRT (DRT + IHT) and control (CON – 30 min of stretching). Interventions occurred 3 times/week for 10 weeks, and ABP was assessed before and after the interventions. ANOVAs and ANCOVAs adjusted for pre-intervention values were employed for analysis. Mean 24-hour, awake and asleep BPs did not change in either group throughout the study (all, $P > 0.05$). Nocturnal BP fall as well as the standard deviation, coefficient of variation and the average real variability of ABP also did not change significantly in either group (all, $P<0.05$). Changes in all these parameters adjusted to the pre-intervention values were also similar among the four groups (all, $p > 0.05$)**.** In treated men with hypertension, 10 weeks of DRT, IHT or CRT does not decrease ABP levels nor change ABP variability.

Keywords: strength training, handgrip, ambulatory blood pressure monitoring, blood pressure variability, hypertension.

SUMARY TABLE

What is known about the topic?

- Ambulatory blood pressure (ABP) is a superior method for diagnosing and managing hypertension, and it is associated with cardiovascular and all-cause mortality.
- Hypertension guidelines recommend dynamic (DRT) and isometric handgrip training (IHT) as complementary strategies for the treatment of hypertension.
- However, the effects of DRT and IHT alone or in combination (CRT) have been poorly investigated in middle-aged men with hypertension.

What this study adds?

- Although being recommended for hypertension treatment, neither DRT, IHT nor CRT changed ABP levels nor ABP variability in middle-aged men with hypertension.
- The absence of effects on ABP parameters does not support the use of DRT, IHT or CRT as isolated exercise therapies for hypertension in this population

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INTRODUCTION

Current guidelines recommend widespread use of ambulatory blood pressure (ABP) for diagnosing and managing hypertension[1–3]. ABP is superior to office blood pressure (BP) due to its capacity to abolish the “white coat effect” and to assess BP during daily activities, allowing the evaluation of relevant clinical parameters related to the mean ambulatory BP levels (i.e. 24-hour, awake and asleep BPs) as well as BP variability during a day (i.e. nocturnal BP fall; 24-hour, daytime and asleep BP variabilities; and average real variability - ARV)[4–8]. These parameters have shown associations with target-organ damage[9], cardiovascular morbidity[4], cardiovascular mortality[5], and all-cause mortality[7] independently from office BP. Therefore, interventions for hypertension treatment need to improve ABP parameters[3,10].

Exercise is an important non-pharmacological therapy for hypertension. Aerobic training is recommended as the primary exercise type for controlling BP[2,3,10] based on its proved efficacy in reducing office as well as ambulatory BPs[11]. Additionally, nowadays, most hypertension guidelines also recommend dynamic resistance training (DRT) as an exercise therapy for patients with hypertension[2,3], and the last American guidelines[10] included isometric handgrip training (IHT) as a recommendation. Nevertheless, the use of DRT and IHT in hypertension is mainly supported by the effects of these training modalities in reducing office BP[12], while their effects on ABP parameters have been poorly investigated.

The randomized controlled trials that have investigated the effects of DRT on ABP in patients with hypertension revealed conflicting results. Two studies[13,14] showed no change in 24-hour, daytime and night-time BPs, while one study found a reduction in 24-hour and daytime BPs[15]. Additionally, in only one of these studies[14], the nocturnal BP fall was improved by DRT. Regarding IHT, none of the four randomized controlled trials conducted with patients with hypertension reported reductions in ABP mean parameters nor improvements in ABP

variability[16–19]. However, a non-controlled trial conducted with normotensives reported a decrease in 24h, daytime and night-time mean BPs[20]. Therefore, the evidence supporting the recommendation of DRT or IHT as exercise therapies for hypertension treatment needs to be improved with well-conducted randomized controlled trials evaluating their effects on ABP parameters.

Dynamic and isometric resistance exercises impose different hemodynamic stimuli during their execution[21–24] and may lead to distinct chronic physiological adaptations. Along this line, some evidence suggests that DRT decreases office BP due to its effects in improving systemic vascular function[25], while the vascular effects of IHT are restricted to the exercised musculature [26–28], and its effect in decreasing office BP has been attributed to autonomic adaptations characterized by decreasing cardiac and peripheral sympathetic modulation[29,30]. Therefore, as DRT and IHT seem to reduce office BP by distinct mechanisms, it is possible to hypothesize that joining them in a combined resistance training (CRT = DRT + IHT) program could stimulate both of these hypotensive mechanisms (reducing sympathetic activity and improving vascular function), producing an additive hypotensive effect that may lead to a reduction in ABP, producing a greater impact of hypertension treatment. Nevertheless, this hypothesis has yet to be examined.

Thus, the aim of this study was to evaluate the effects of DRT, IHT, and CRT on ABP levels and variability in treated middle-aged men with hypertension. Based on the previous rationale, the hypotheses were that DRT and IHT alone would not change ABP parameters, while their combination in a CRT would reduce ABP levels and improve ABP variability.

METHODS

Participants

Patients' recruitment occurred from September 2018 to November 2021. Due to the COVID-19 pandemic, the study´s procedures had to be interrupted or restricted from March 2020 to September 2020 and from March 2021 to June 2021. Two hundred and nineteen middle-aged treated men with hypertension were invited to participate in this study, and 96 signed the informed written consent after being informed about the benefits and risks of the study. The data collected for this study were part of a bigger trial registered at the Brazilian Clinical Trials (RBR-4fgknb at http://www.ensaiosclinicos.gov.br) and approved by the Ethics Committee of the School of Physical Education and Sport, University of São Paulo (CAAE process 2.870.688). The results regarding the effects of DRT, IHT and CRT on office BP and its mechanisms have already been published[31]. The sample of the present study consisted of the patients included in the previous study who had also undergone ABP monitoring.

The inclusion criteria were: i) males; ii) aged between 30 and 65 years old; iii) have hypertension; iv) be under consistent antihypertensive medication with dosage and medication maintained at least for the previous 4 months; and v) do not practice more than 150 min/week of physical activity, do not participate in any regular exercise program, and have not practiced resistance training in the last six months**.** The exclusion criteria were: i) presence of secondary hypertension or target-organ damage; ii) use of nondihydropyridine calcium channel blockers, beta-blockers, or insulin; (iii) presence of other cardiovascular disease, obesity level II or more, diabetes with complications, and clinical conditions that preclude resistance training; (iv) presence of electrocardiographic alterations during exercise; and ix) have office systolic BP (SBP) ≥ 160 mmHg and/or diastolic BP (DBP) ≥ 105 mmHg. Furthermore, during all the study, the patients

were asked about any change in medication treatment and physical activity level. If there was any change in these parameters, the patient would be excluded from the study.

Preliminary Procedures

Adherence to the study criteria was checked by preliminary procedures. As recommended by the Brazilian Hypertension Guidelines [2], the patients who volunteered to participate were interviewed regarding their health history and medication use, were clinically examined by a physician (pain complains, pulse palpation, heart auscultation, etc) to assess health conditions that may preclude resistance training (e.g. cardiac abnormalities and musculoskeletal disorders), and had their blood and urine collected to assess cardiovascular risk factors and target-organ damage. Complementary exams were requested when necessary. The patients were also asked about their exercise practice in the last 6 months and completed the International Physical Activity Questionnaire[32]. Their weight and height were measured, and body mass index was calculated[33]. Their office BP was assessed on two different occasions. On each occasion, BP was measured in both arms, and BP measurements were taken three times in each arm using the auscultatory method and ensuring an interval of at least 1 minute between the measurements. The mean of the six measurements taken in each arm (2 occasions with 3 measures in each) was calculated, and the highest mean BP value obtained between the arms was considered as the patient´s office BP [2]. Finally, the patients underwent a maximal cardiopulmonary exercise test to assess cardiovascular function and physical fitness. The test was conducted on a cycle ergometer with a 15 watts/min protocol until voluntary exhaustion. Heart rate was monitored via ECG, auscultatory BP was measured every 2 min, and oxygen consumption (VO_2) was assessed using a metabolic cart (Medical Graphics Corporation, CPX Ultima, Minnesota, USA) .

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148 *Study Design*

149 This study was a randomized controlled trial with four-parallel groups. It was designed to evaluate
150 and compare the effects of DRT, IHT and CRT on ABP. For that, each patient initially underwent a
151 pre-intervention ABP monitoring. Then, each patient was randomly allocated into one of four
152 groups (DRT, IHT, CRT or control – CON) with a 1:1:1:1 allocation ratio and participated in the
153 specific intervention designed for his group for 10 weeks. Finally, 48 to 96 hours after the last
154 intervention session, the patient underwent a post-intervention ABP monitoring. Data obtained in
155 pre- and post-intervention ABP monitoring of the patients of the 4 groups were compared. The
156 main outcome of the study was mean ABP level, and the secondary outcome was ABP variability.

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158 *Measurements*

159 ABP monitoring was initiated between 8 and 10 a.m. An adequate cuff size for the arm
160 circumference was chosen and placed on the non-dominant arm of the patients. As BP variability
161 was a secondary outcome of the present study, the ABP monitor (Spacelabs Medical, Model
162 90207) was programmed to take measures every 15 min for 24 hours [34]. During the monitoring,
163 the patients were instructed to keep their regular daily activities, not to exercise, not to sleep
164 during the day, and not to ingest alcohol. Additionally, they were asked to record their activities
165 throughout the day, such as the time of waking-up, sleeping, meals, medication use and other
166 relevant events (e.g., working, commuting and adverse events). For the post-intervention ABP
167 monitoring, the patients were instructed to keep a similar daily routine to the pre-intervention
168 monitoring.

169 For data analysis, only recordings with at least 80% of valid measures were analysed [35]. ABP
170 levels were determined by the mean of all BPs recorded during the 24-hour period as well as the

means of all BPs recorded during the awake and the asleep periods reported by each patient [35]. ABP variability was defined as suggested in literature [34] using by the following parameters:

i) nocturnal BP fall calculated by the difference between awake and asleep BPs divided by the awake BP and multiplied by 100, following the equation [34]:

$$Nocturnal\ BP\ fall = \frac{(awake\ BP - asleep\ BP)}{Awake\ BP} \times 100$$

ii) standard deviation (SD) of the measurements recorded during the 24-hour recording period [34,36], calculated as:

$$SD = \sqrt{\frac{1}{N-1} \sum_{i=1}^{N} (BPi - \overline{BP})}$$

were $\boldsymbol{N}$ = ambulatory BP readings, and $\overline{\boldsymbol{BP}}$ = the mean of the recording values.

iii) coefficient of variation (CV) of ABP calculated by the quotient between the SD and the mean BP of the recording period, following the equation [34]

$$CV = 100 \times \frac{SD}{\overline{BP}}$$

iv) the average real variability (ARV) calculated by the following equation:

$$ARV = \frac{1}{\sum w} \sum_{k=1}^{n-1} w \times |BP_{k+1} - BP_k| \quad .$$

where “k” ranges from 1 to N-1, “w” is the time interval between the consecutive measurements and “n” the number of measurements [7,34].

Interventions

The intervention protocol was conducted 3 times per week for 10 weeks in all groups. All patients were instructed not to change their daily physical activity during the study period except for the inclusion of the intervention proposed for his group. For all interventions, including the control group, training adherence was calculated based on the percentage of the planned sessions completed by each patient, and only results from patients who completed at least 80% of the planned sessions (i.e., 24 out of 30 sessions) were considered for analyses. The DRT protocol followed the recommendations of the hypertension guidelines[10,37]. In each training session, the patients executed 8 dynamic resistance exercises (chest-press, leg-press, lat pull-down, left knee extension, right knee extension, elbow flexion, left knee flexion and right knee flexion). In each exercise, they performed 3 sets of repetitions until moderate fatigue (i.e., a reduction of movement velocity) with 90 s interval between the sets and the exercises. The intensity was set at 50% of 1 repetition maximal (1RM) measured before the beginning of the study, and workload was increased by 5–10% when the patient was able to perform more than 15 repetitions without moderate fatigue in two consecutive sets [38]. Each training session lasted around 30 to 40 minutes.

The IHT protocol followed the protocol recommended by the American guidelines[10] and used an automatic digital handgrip (ZonaPlus, Zona Health, Boise, Idaho, USA). In each session, the

patients executed 4 sets of 2 min isometric contraction at 30% of MVC alternating between hands (i.e., 2 sets with each hand) with 60 s interval between the sets. MVC for both hands was measured at the beginning of each training session. Each training session lasted 12 minutes.

The CRT protocol was composed of both the IHT and DRT protocols. Thus, in each training session, the patients always executed the DRT protocol first followed by the IHT protocol. Training sessions lasted around 42 to 52 minutes.

The CON group executed a stretching intervention that has already been shown not to alter BP[39]. In each session, the patients stretched for 30 min, executing 20 to 25 exercises, and in each exercise, they performed 2 to 3 movements, holding each stretch for 20–30 s at the highest degree of stretching without pain.

Statistical Analysis

The minimal sample size calculated for this study (G*Power 3,1,9,2, Univeritat Kiel, Kiel, Germany) was 56 subjects (14 in each group) based on 24-hour SBP and considering 0.23 as the expected effect size[13,16], a statistical power of 80%, and an alpha value of 0.05.

Data presented normal distribution as checked by Shapiro–Wilk test, and no outlier value was identified by box plots. The groups' characteristics were compared by one-way ANOVAs for continuous variables and by Pearson's χ^2 test for categorical variables. The efficacy of interventions on the study's outcomes was analysed by two-way mixed ANOVAs considering group as a between main factor (DRT vs. IHT vs. CRT vs. CON) and time (pre- vs. post intervention) as a within main factor. When significant main effects or interactions were observed, pairwise comparisons were performed using Newman-Keuls post-hoc tests. Additionally, changes obtained with the interventions (Δ = post-intervention – pre-intervention) adjusted for pre-intervention values were compared between the groups by ANCOVAs, and Bonferroni post-hoc

tests were applied for pairwise comparisons when a significant effect was observed. For ANOVAs, data are presented as mean ± standard deviation, while for ANCOVAs, data are presented as mean difference and 95% confidence interval. The null hypothesis was rejected for values of $p<0.05$. All statistical analyses were performed with IBM© SPSS© version 25.0

RESULTS

From the 96 subjects who signed the inform consent for participating, 21 were exclude for not accomplishing with the study criteria (1 for being diagnosed with neoplasia, 1 for being diagnosed with heart diseases, 3 for withdrawing due to the COVID-19 pandemic, 1 for being diagnosed with secondary hypertension, 1 for taking leave due to a surgical procedure, 7 for being unavailable to attend evaluations, 1 for presenting with target organ damage, 1 for unspecified personal reasons, 3 for changing the class of antihypertensive medication, and 1 for having SBP/DBP values greater than 160/105). Thus, 75 patients began the preliminary procedures, of which 5 were excluded (1 due to the COVID-19 pandemic, 1 for experiencing joint pain during the 1RM test, and 3 for being unavailable to attend the stages of the preliminary procedures). Subsequently, 70 subjects were randomly allocated into the study's groups, and 11 (15.7%) dropped out during the intervention period. Two patients were excluded from DRT group (1 for being diagnosed with cardiovascular disease by an external physician and 1 for unspecified personal reasons), 3 from the IHT group (2 for not adhering to the training and 1 for changing the class of antihypertensive medication), 4 from the CRT group (1 for not adhering to the training, 2 for unspecified personal reasons, and 1 for presenting orthopedic limitations), and 2 from the CONT group (1 due to the COVID-19 pandemic and 1 for unspecified personal reasons).

So, 59 patients finished the experimental protocol (Figure 1, DRT = 15, IHT = 15, CRT = 14, and CON = 15). All these patients attended for at least 80% of the intervention sessions, with an

average adherence of 89±7% in the DRT, 90±9% in the IHT, 89±7% in the CRT, and 88±9% in the CON (p = 0,921). Patients from the four groups presented similar initial characteristics, including: age, anthropometric characteristics, physical activity and fitness levels, office BP and pharmacological treatment (Table 1).

None of the interventions changed left nor right isometric handgrip MVCs. Conversely, DRT and CRT significantly increased 1RM in all exercises (bench press: +16±13% and +17±11%; leg press: +23±14% and +24±19%; lat pull down: +22±12% and +24±19%; left leg extension: +20±18% and +22±20%; right leg extension: +18±20% and +19±19%; arm curl: +23±17% and +12±26%; left leg curl: +25±9% and +20±9%; and right leg curl: +26±9% and +18±10% for DRT and CRT, respectively, all $p < 0.05$), while no change was observed for the IHT and the CON groups.

Mean 24-hour, awake and asleep SBP and DBP did not change from the pre- to the post-intervention evaluation in any group (all $p > 0.05$, Table 2). Additionally, the mean 24-hour, awake or asleep SBP and DBP changes adjusted to the pre-intervention values were not different among the four groups (all $p > 0.05$, Figure 2).

Nocturnal SBP and DBP falls also did not change from the pre- to the post-intervention evaluation in any group (all $p > 0.05$, Table 2). Additionally, changes in these variables adjusted to the pre-intervention values were similar in the four groups (all > 0.05, Figure 3), except for the change in SBP fall that was slight greater in the DRT group than in the CRT ($p=0.045$).

Concerning ABP variability, 24-hour, awake and asleep SD and CV as well as ARV for SBP and DBP did not change from the pre- to the post-intervention evaluation in any group (all $p > 0.05$, Table 2), and the changes of these parameters adjusted to the pre-intervention values were not different among the groups (all $p >0.05$, Figure 4).

DISCUSSION

The main findings of this study are that although being recommended for hypertension treatment, neither DRT, IHT nor CRT changed ABP levels nor variability in treated middle-aged men with hypertension.

Considering DRT, current meta-analytic data show its efficacy in reducing office SBP/DBP by -5,7/-5,2 mmHg in patients with hypertension[40] . Indeed, in the present trial, we also found a significant reduction in office SBP by −8.4 [95%CI: −15.9 to −0.8] mmHg after DRT [31]. Nevertheless, the present data showed that neither systolic nor diastolic ABP parameters were changed by DRT in middle aged men with treated hypertension. This absence of a hypotensive effect of DRT on ABP is in accordance with two previous studies that have investigated other samples of patients with hypertension [13,14]. Bertani et al.[14] studied elderly patients with hypertension and Blumenthal et al.[13] studied non-medicated men with hypertension. Thus, the replication of these results in different populations with hypertension strengthens the evidence that DRT alone may not change ABP. On the other hand, one study [15] reported a decrease in 24-hour and daytime BP after DRT in patients with hypertension, but this decrease did not differ from the control group, indicating that the reductions in 24-hour and daytime BP did not resulted from the DRT per se. Therefore, the present and previous findings suggest that DRT decreases office, but not ambulatory BP in patients with hypertension.

IHT was also not effective in reducing ABP for the awake, asleep or 24-hour period, and this absence of effect is in accordance with the three previous studies conducted with patients with hypertension[16–18]. Thus, the replication of this finding in different populations with hypertension (i.e., men and women, middle-aged and elderly, with and without medication use) strengthens the evidence that IHT alone may not change ABP. A recent large-scale pairwise and network meta-analysis pointed out IHT as the most effective exercise modality for reducing BP

[41]. However, these results considered office BP, and as pointed out by the authors and also by a discussion paper [42], they should be taken with caution because they were based on a small number of trials. Therefore, the present results contribute to this discussion, reinforcing the concern regarding the recommendation of IHT as an alone treatment for men with hypertension, since its effects decreasing office BP still need more studies and its effects decreasing ABP (that presents a stronger association with hypertension morbimortality) are not evident in the literature.

In contrast to the present study´s hypothesis, CRT also did not modify mean ABP parameters (i.e., 24-hour, awake and asleep BP). The rationale for the present study's hypothesis was that dynamic resistance exercise and isometric handgrip promote distinct acute cardiovascular stimuli during their execution[21,22] and, consequently, may provide distinct chronic cardiovascular adaptations, with DRT inducing vascular improvements[25,43] and IHT autonomic adaptations[26,30]. Nevertheless, the absence of ABP changes after CRT show no additive effect of DRT and IHT. Actually, in the bigger study from which the present data derived, CRT induced the same decrease in office BP as DRT, and both training regimens only improved microvascular function, while IHT had no effect on hemodynamic, vascular or autonomic mechanisms [31]. Therefore, as the hypotensive mechanisms of DRT and IHT were not additive in CRT, the combination of IHT and DRT did not potentiate the office BP-lowering effect of DRT, and consequently, did not induce a decrease of ABP levels.

Neither DRT, IHT or CRT changed any of the ABP variability parameters assessed in the present study. Despite the relevance of ABP variability on cardiovascular prognosis[6,7], the effects of exercise training on BP variability has been poorly studied. To the best of our knowledge, only one previous investigation with patients with hypertension reported an increase in nocturnal BP fall with DRT[14], while another study[19] reported no change in AVR after IHT. Thus, the present study's findings contribute to increase the knowledge in this area by showing no effect of DRT,

IHT or CRT on different short and long-term ABP variability parameters in patients with hypertension.

An important aspect to be discussed is the fact that DRT and CRT decreased office BP in our previous study [31], but did not decrease ABP in the present study. This discrepancy may be related to the sensitivity of ABP to respond to interventions due to the greater variability of BP. Office BP is assessed under highly controlled conditions (time and temperature are monitored, and there is less noise)[2], while ABP measurements occur during the execution of daily activities in the community with the patients exposed to different environmental situations[35]. Thus, the greater ABP variability may have masked/blunted the BP-lowering effect of the training regimens. Actually, a previous meta-analysis showed that both pharmacological [44] and non-pharmacological [39,45] treatments induced smaller effect sizes for ambulatory than office BP reductions. Besides not been significant, the mean decreases observed in 24-hour, awake and asleep BP after DRT, IHT and CRT were not considered clinically relevant, since they were below 5 mmHg, a cutoff point related to 10% decrease in cardiovascular risk [46].Some other aspects may be raised to explain the lack of effect of resistance training on ABP. The fact that the sample was medicated and well-controlled (70% of the whole sample presented 24-hour SBP <130 mmHg and 42% 24-hour DBP < 80 mmHg) [47] may have blunted the training BP-lowering effect since it is known that this training effect is greater in patients with higher baseline BP [11]. Additionally, it is possible that a longer period of training is necessary to reduce ABP compared to office BP. Along this line, a study that has investigated aerobic training in patients with hypertension reported no ABP change after 6 months of training but a significant decrease after 12 months[48]. Therefore, future studies aiming to evaluate ABP parameters after resistance training should consider less controlled sample and a longer period of training.

The results obtained in the present study have important clinical applications. Considering the clinical relevance of ABP [4,8,49], the absent effect of resistance training on ABP parameters

reinforces the need for caution when applying in clinical settings and guidelines, the results from studies that have only investigated office BP, and they also highlight the importance of including ABP in future studies. Therefore, the absence of reduction in ABP (i.e. a better risk marker than office BP in hypertension) with DRT, IHT and CRT does not support their recommendation as isolated exercise therapies in men with hypertension, reinforcing their use as a complementary therapy to aerobic training. Additionally, the present results do not support the combination of DRT and IHT for potentiating the BP reduction in men with hypertension.

Limitations

This study has some limitations that must be highlighted. Firstly, the sample consisted of middle-aged men with treated hypertension. The choice for only including men was done by convenience and imposes limitations for the extrapolation of the results to women, being important to recognize the importance of future investigations to study women. Second, the patients were taking medication and using different antihypertensive drugs that might differently influence the results. These medication characteristics were chosen to increase the applicability of the results in men as hypertensive guidelines [1–3]recommend pharmacological treatment for most of the patients and, in clinical practice, these patients were usually taking more than one antihypertensive drug. Third, the absence of significant effects of training on ABP parameters may raise concern regarding a small sample size. However, the sample size was greater than calculated a priori for this study, and the absence of significant effects actually expressed the large variability of responses among the patients, with some of them presenting expressive decreases and others increases in ABP after the training which may be expected for ABP parameters and was considered in sample size calculation. Future studies should investigate the factors related to responsiveness to resistance training, but as discussed before, the fact that the present sample was well-controlled by medication may have influenced the results, precluding a greater BP reduction, which should be investigated in the future. Finally, the results are

dependent on the specific training protocols employed in the present study, and different responses may be obtained with other modalities or intensities of resistance training. However, the training protocols applied in the present study are in accordance with the protocols recommended by the hypertension guidelines[1,2,10,54]. Nevertheless, as discussed before, a longer training period may lower ABP, which should be investigated in the future.

CONCLUSION

In conclusion, in middle-aged men with hypertension, 10 weeks of DRT, IHT or CRT do not decrease ABP levels nor variability, not changing mean 24-hour, awake or asleep BPs nor nocturnal BP fall or any other ABP variability parameter.

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559 **FIGURE LEGENDS**

560 Figure 1. Flow diagram of the trial. ABPM = ambulatory blood pressure monitoring; DRT =
561 dynamic resistance training; IHT = isometric resistance training; CRT = combined resistance
562 training; CON = control

563

564 Figure 2. Between-group comparisons of the changes (post-intervention – pre-intervention)
565 observed in each mean ambulatory blood pressure parameter adjusted for the pre-intervention
566 value. SBP = Systolic blood pressure; DBP = diastolic blood pressure; DRT = dynamic resistance
567 training; IHT = isometric handgrip training; CRT = combined resistance training; CON = control
568 group. Data as mean difference and 95% confidence interval for difference. Analysis: one-way
569 ANCOVAs.

570

571 Figure 3. Between-group comparisons of the changes (post-intervention – pre-intervention)
572 observed in nocturnal blood pressure fall adjusted for the pre-intervention value. SBP = Systolic
573 blood pressure; DBP = diastolic blood pressure; DRT = dynamic resistance training; IHT =
574 isometric handgrip training; CRT = combined resistance training; CON = control group. Data as
575 mean difference and 95% confidence interval for difference. Analysis: one-way ANCOVAs.

576

577 Figure 4. Between-group comparisons of the changes (post-intervention – pre-intervention)
578 observed in each ambulatory blood pressure variability parameter adjusted for the pre-
579 intervention value. SBP = Systolic blood pressure; DBP = diastolic blood pressure; DRT =
580 dynamic resistance training; IHT = isometric handgrip training; CRT = combined resistance
581 training; CON = control group; SD = standard deviation; CV = coefficient of variation; ARV =

582 average real variability. Data as mean difference and 95% confidence interval for difference.

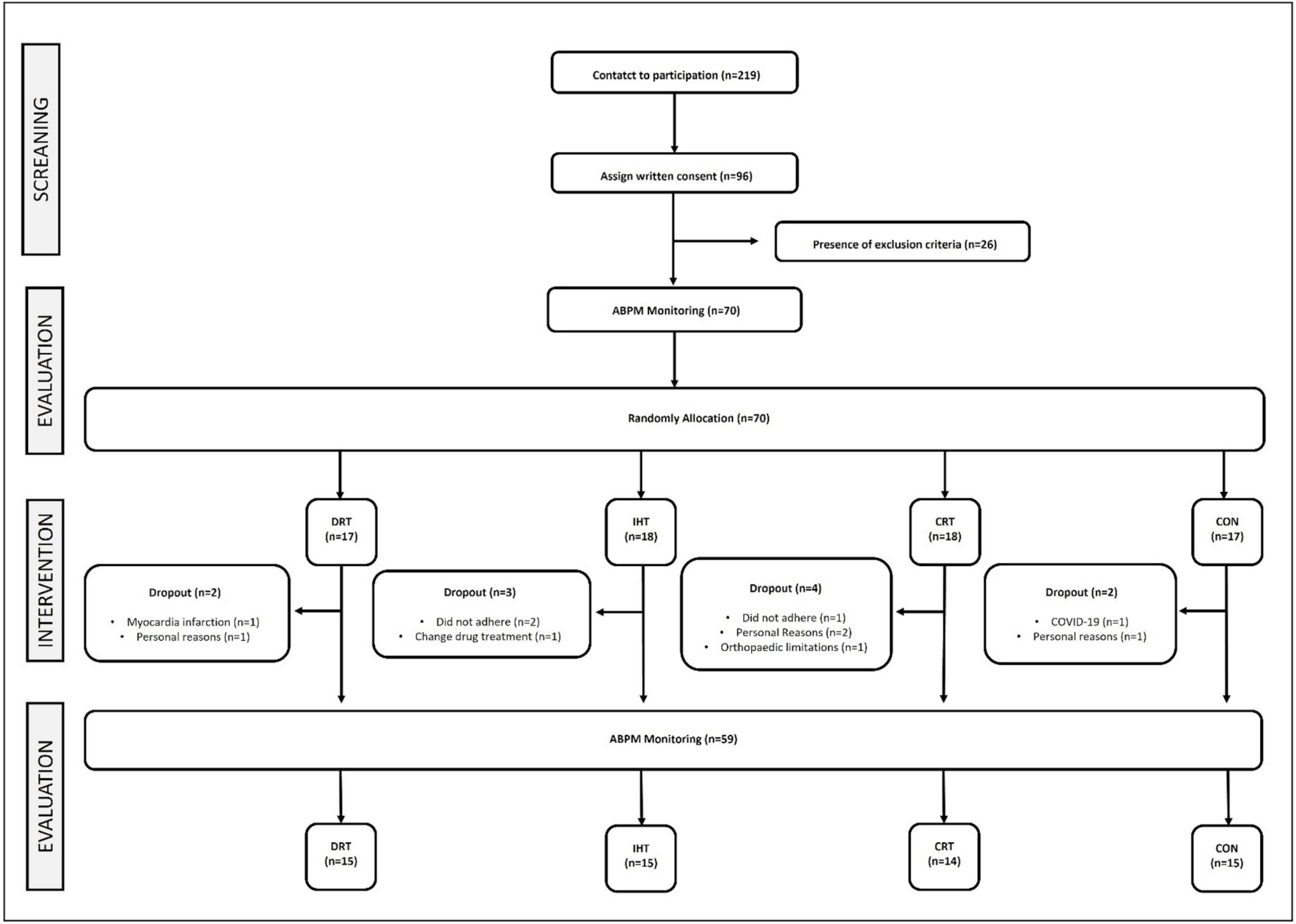
583 Analysis: one-way ANCOVAs.

584

TABLE LEGENDS

Table 1. Patient's characteristics

Table 2. Ambulatory blood pressure parameters assessed in the pre- and the post-intervention evaluations in each group as well as changes (post-intervention – pre-intervention) obtained in each group.



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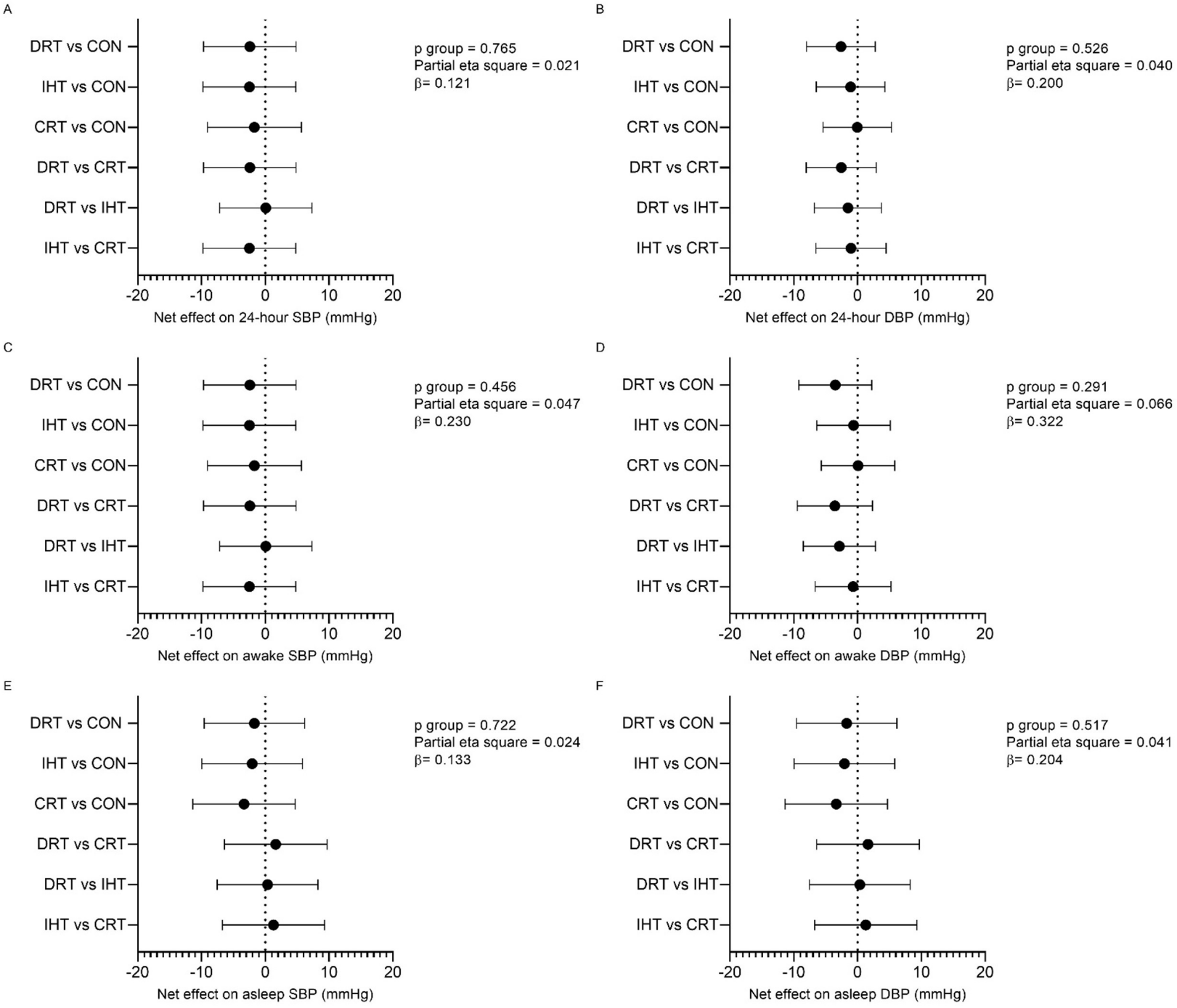

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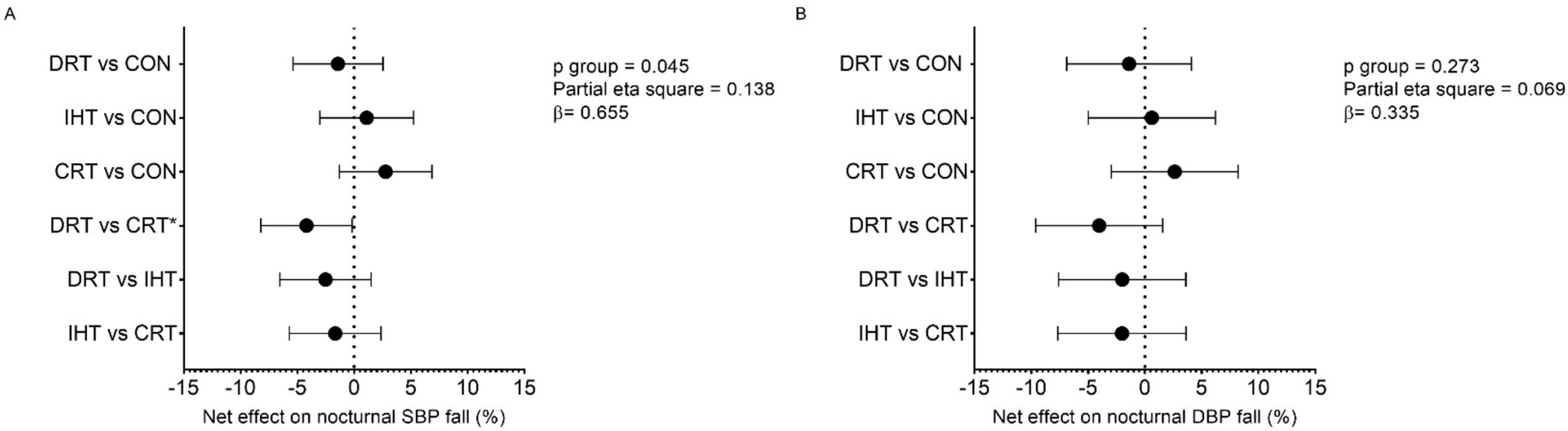

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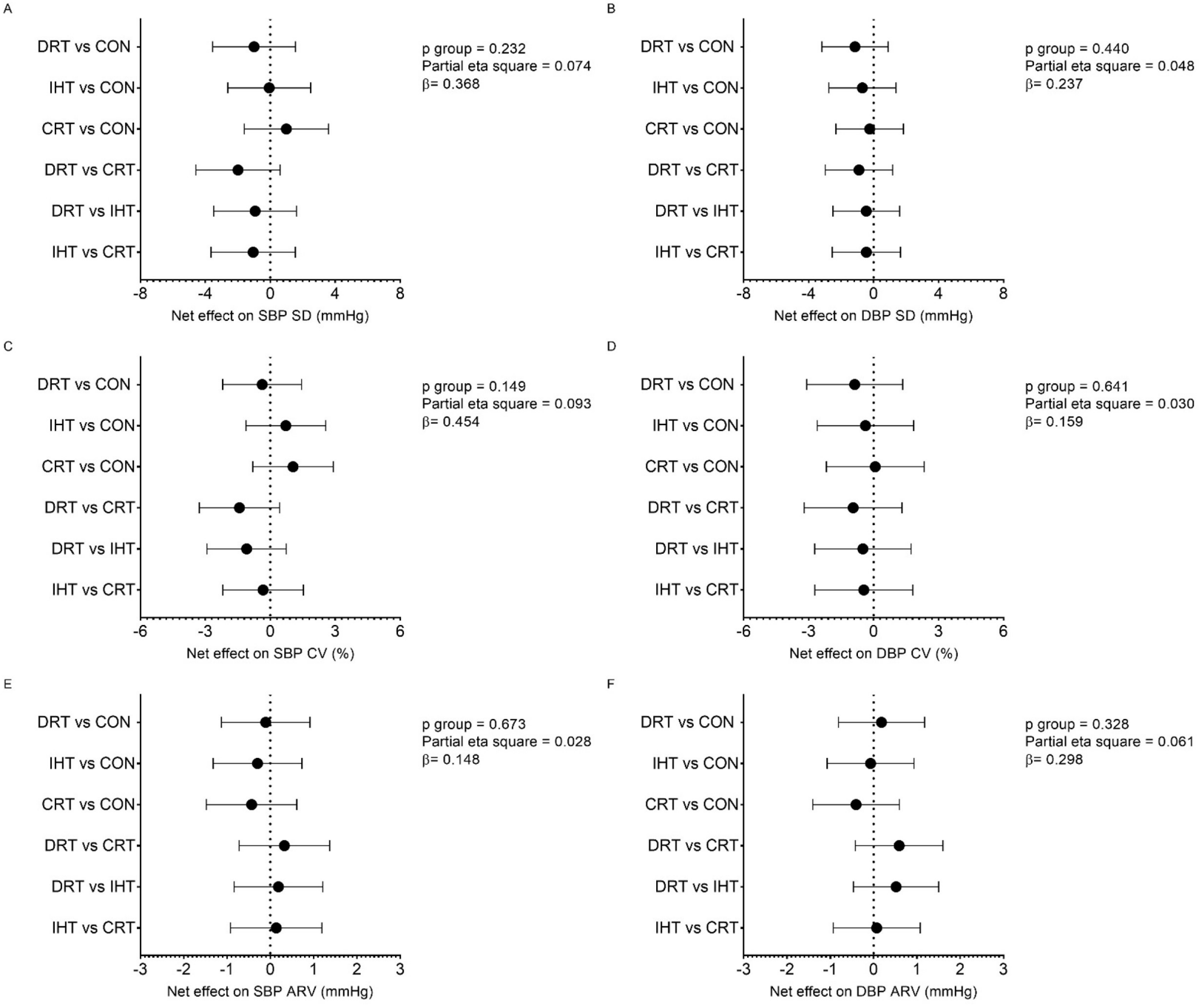

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Table 1. Patient's characteristics

	DRT	IHT	CRT	CON	P
N	15	15	14	15	
Age (years)	54±7	55±7	51±11	53±9	0.566
Previous COVID-19 without hospitalization – n(%)	2 (13)	1 (7)	1 (7)	1 (7)	1.000
Anthropometric					
Height (cm)	175±6	174±8	178±10	175±6	0.568
Weight (kg)	91±12	86±15	90±18	89±12	0.738
BMI (kg/m^2)	29.8±3.5	28.1±3.5	28.4±3.8	29.3±3.7	0.550
Physical Activity and Fitness					
Total physical activity (minutes/week)	40±44	57±55	38±41	61±50	0,453
VO_2 peak ($ml.kg^{-1}.min^{-1}$)	22,8±3,9	20,1±4,1	21,8±5,4	20,6±2,0	0.558
Office blood pressure					
SBP (mmHg)	130±12	131±13	132±10	127±11	0.648
DBP (mmHg)	88±9	88±7	87±8	85±7	0.584
Pharmacological treatment					
Antihypertensive Monotherapy	9 (60)	8 (53)	6 (43)	9 (60)	0.844
Antihypertensive Polytherapy	7 (47)	7 (47)	8 (57)	6 (40)	
ARB - n(%)	11 (73)	9 (60)	10 (71)	9 (60)	0.904
ACEi - n(%)	2 (13)	1 (7)	3 (21)	3 (20)	0.674
CCB - n(%)	5 (33)	5 (33)	6 (43)	6 (40)	0.906
Diuretics – n(%)	6 (40)	6 (40)	5 (36)	3 (20)	0.653

Data: mean ± standard deviation or number (percentage). DRT = dynamic resistance training; IHT = isometric handgrip training; CRT = combined resistance training; CON = control; COVID-19 = coronavirus disease 2019; VO_2 peak = peak oxygen consumption; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; ARB = angiotensin receptor blocker; ACEi = angiotensin-converting enzyme inhibitor; CCB = calcium channel blocker. Analysis: one-way ANOVAs for continuous variables and Pearson's X^2 test for categorical variables.

Table 2. Ambulatory blood pressure parameters assessed in the pre- and the post-intervention evaluations in each group as well as changes (post-intervention – pre-intervention) obtained in each group.

Ambulatory blood	Dynamic Resistance Training			Isometric Handgrip Training			Combined Resistance Training			Control Group			P		
pressure parameter	Pre	Post	Δ	Pre	Post	Δ	Pre	Post	Δ	Pre	Post	Δ	Group	Time	Interaction
Mean BP (mmHg)															
24-hour SBP	126 ± 8	124 ± 8	-2 ± 6	127 ± 11	125 ± 7	-2 ± 8	125 ± 7	124 ± 6	0 ± 4	125 ± 7	124 ± 6	2 ± 11	0.973	0.542	0.580
24-hour DBP	82 ± 5	79 ± 5	-3 ± 4	82 ± 6	81 ± 6	-1 ± 6	78 ± 5	79 ± 6	1 ± 4	79 ± 7	80 ± 8	1 ± 7	0.542	0.535	0.217
Awake SBP	131 ± 9	128 ± 9	-3 ± 6	133 ± 13	131 ± 11	-2 ± 9	130 ± 7	130 ± 7	0 ± 4	128 ± 11	130 ± 11	2 ± 11	0.853	0.475	0.268
Awake DBP	87 ± 6	83 ± 6	-4 ± 5	88 ± 7	86 ± 6	-1 ± 7	83 ± 5	84 ± 6	1 ± 4	84 ± 9	85 ± 9	1 ± 8	0.488	0.410	0.102
Asleep SBP	113 ± 8	113 ± 7	0 ± 5	111 ± 15	111 ± 15	0 ± 6	111 ± 8	111 ± 7	-1 ± 7	112 ± 12	114 ± 13	2 ± 13	0.801	0.783	0.824
Asleep DBP	71 ± 6	69 ± 2	-2 ± 5	68 ± 8	69 ± 9	1 ± 5	67 ± 6	67 ± 6	0 ± 5	68 ± 9	70 ± 11	2 ± 10	0.626	0.883	0.360
Nocturnal BP fall (%)															
SBP	13 ± 4	11 ± 4	-3 ± 4	17 ± 7	15 ± 7	-2 ± 4	15 ± 5	15 ± 5	1 ± 4	13 ± 5	11 ± 2	-1 ± 5	0.072	0.058	0.222
DBP	18 ± 6	16 ± 15	-2 ± 6	22 ± 8	20 ± 9	-2 ± 5	19 ± 7	21 ± 7	2 ± 6	18 ± 8	17 ± 6	0 ± 8	0.232	0.473	0.403
ABP variability															
SBP SD (mmHg)	12 ± 3	11 ± 2	-1 ± 2	13 ± 3	13 ± 3	0 ± 2	12 ± 2	13 ± 2	1 ± 2	12 ± 3	12 ± 2	0 ± 3	0.444	0.670	0.171
DBP SD (mmHg)	11 ± 3	10 ± 2	0 ± 2	12 ± 3	11 ± 3	0 ± 2	11 ± 3	11 ± 2	0 ± 2	11 ± 2	11 ± 3	1 ± 3	0.850	0.877	0.379
SBP CV (%)	10 ± 2	9 ± 2	-1 ± 2	11 ± 3	11 ± 4	0 ± 2	10 ± 2	11 ± 2	1 ± 1	10 ± 2	10 ± 2	0 ± 2	0.431	0.688	0.271
DBP CV (%)	13 ± 3	13 ± 2	0 ± 2	14 ± 3	14 ± 4	0 ± 2	14 ± 3	14 ± 2	1 ± 3	14 ± 3	14 ± 3	0 ± 3	0.840	0.915	0.709
SBP ARV (mmHg)	7 ± 1	8 ± 1	0 ± 1	8 ± 1	8 ± 1	0 ± 1	7 ± 1	7 ± 1	0 ± 1	7 ± 1	8 ± 1	0 ± 1	0.436	0.347	0.835
DBP ARV (mmHg)	7 ± 1	7 ± 1	0 ± 1	6 ± 1	6 ± 1	0 ± 1	6 ± 1	6 ± 1	0 ± 1	6 ± 1	6 ± 1	0 ± 1	0.244	0.893	0.556

Data: mean ± standard deviation. SBP = systolic blood pressure; DBP = diastolic blood pressure; SD = standard deviation; CV = coefficient of variation; ARV = average real variability. Analysis: two-way mixed ANOVAs.