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ORIGINAL ARTICLE

Hemodynamic responses to different isometric handgrip protocols in hypertensive men

Réponses hémodynamiques à différentes variétés de préhension isométrique chez des hypertendus de sexe masculin

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Summary

Objectives. – Several previous studies have shown that regular isometric handgrip (IHG) exercise reduces blood pressure in hypertensive individuals. The aim of this study was to investigate the responses of hemodynamic variables to five IHG protocols of different combinations but similar workloads.

Equipment and methods. – Fifteen sedentary men with pre to stage 1 hypertension (Mean \pm SD; age, 46 ± 6 years, systolic blood pressure [SBP], 138 ± 7 mmHg; DBP, 89 ± 6 mmHg) completed five IHG protocols randomly on five separate sessions including 8×30 s at 60% of MVC (high intensity high frequency [HIHF]); 4×1 min at 60% of MVC (high intensity low frequency [HILF]); 8×1 min at 30% of the MVC (low intensity high frequency [LIHF]); 4×2 min at 30% of MVC (low intensity low frequency [LILF]) and 8×1 min at 3% of MVC (Sham). Blood pressure and heart rate were measured at rest and at 0, 5, 10, 15, 30, 45 and 60 minutes of recovery. Plasma lactate levels were determined at rest and immediately after exercise.

Results. – The highest increase in SBP was found immediately following HILF protocol and it was significantly ($P < 0.01$) different than HIHF and sham trials. HR in LIHF was significantly greater compared to HILF and sham ($P < 0.01$). During recovery, a significant post-exercise hypotension (PEH) was observed for all trials irrespective of the trial type ($P < 0.05$). However, PEH

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MOTS CLÉS

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was significantly ($P < 0.01$) greater following HIHF compared to HILF at 15 minutes (-8 mmHg) and 30 minutes (-12 mmHg). Plasma lactate after last contraction was significantly higher in HIHF ($P < 0.05$) and HILF ($P < 0.01$) protocols compared to LIHF protocol, though there was no significant correlation between responses of plasma lactate and SBP ($P > 0.05$).

Conclusion. – These findings suggest that different IHG protocols of similar workloads affect hemodynamic variables differently, and that hemodynamic changes during and after IHG are related to the frequency and duration of contractions.

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Résumé

Objectifs. – Plusieurs études précédentes ont montré qu'un exercice de préhension isométrique (IDP) réduisait la pression artérielle chez les personnes hypertendues. Le but de cette étude était d'étudier les réponses des variables hémodynamiques à cinq protocoles IDP de combinaisons différentes, mais avec des charges de travail similaires.

Matériel et méthodes. – Quinze hommes sédentaires présentant une hypertension artérielle au stade pré-HTA ou au stade 1 (moyenne \pm écart-type ; âge, 46 ± 6 ans, pression artérielle systolique [TAS], 138 ± 7 mmHg ; TAD, 89 ± 6 mmHg) ont suivi cinq protocoles IDP de façon randomisée au cours de cinq sessions distinctes : 8×30 secondes à 60 % de MVC (haute intensité haute fréquence [HIHF]) ; 4×1 min à 60 % de MVC (haute intensité basse fréquence [HIBF]) ; 8×1 min à 30 % du MVC (basse intensité haute fréquence [BIHF]) ; 4×2 min à 30 % de MVC (basse intensité basse fréquence [BIBF]) et 8×1 min à 3 % de MVC (Sham). La pression artérielle et la fréquence cardiaque ont été mesurées au repos et à 0, 5, 10, 15, 30, 45 et 60 minutes de récupération. Le niveau des lactates dans le plasma ont été déterminés au repos et immédiatement après l'exercice.

Résultats. – La pression artérielle systolique a augmenté pendant le HIBF par rapport au HIHF ($p < 0,01$) et sham ($p < 0,01$). La FC dans le BIHF était significativement plus grande comparée au HIBF ($p < 0,01$) et au sham ($p < 0,01$). Pendant la récupération, une hypotension post-exercice significative (PEH) a été observée pour tous les protocoles, sans tenir compte du type de protocole ($p < 0,05$). Cependant, la PEH était significativement plus élevée ($p < 0,01$) après le HIHF par rapport au HIBF à 15 minutes (-8 mmHg) et à 30 minutes (-12 mmHg). Après la dernière contraction, la lactatémie était significativement plus élevée dans les protocoles HIHF ($p < 0,05$) et HILF ($p < 0,01$) par rapport au protocole LIHF, bien qu'il n'y ait pas de corrélation significative entre les réponses de lactatémie et de la PAS ($p < 0,05$).

Conclusion. – Ces résultats suggèrent que différents protocoles IDP avec des charges de travail similaires affectent différemment sur les variables hémodynamiques et que les changements hémodynamiques sont liés à la fréquence et à la durée des contractions pendant et après IDP.

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1. Introduction

Hypertension is the most important and modifiable cause of cardiovascular disease that affects more than one billion people worldwide and increases the global burden of chronic diseases and mortality [1]. Lifestyle modifications such as regular exercise have been employed [2] to prevent and control high blood pressure (BP). Aerobic exercise all days of the week is recommended to lower resting BP chronically [3]. However, the adherence to this type of training particularly in patients is not very good [4].

In addition, several studies have reported that isometric exercise training (IET), especially isometric handgrip (IHG) exercise may elicit greater BP reduction than dynamic aerobic and resistance exercise [5–8], while the volume of IHG is significantly less and can be performed anywhere and

anytime with high adherence [9–15]. IHG training has been recently classified and recognized by the American Heart Association as a possible therapy for hypertensive patients [16].

Studies that investigated the acute effect of isometric exercise have reported decreases [12,15,17] or no changes [9,13,14] in hemodynamic parameters. Most of these studies utilized a handheld dynamometer and four 2 minutes efforts at moderate intensity (30% maximal voluntary capacity [MVC]), interspersed by 1 to 3 minutes rest [12,14,15,17,18]. The discrepancy in the literature has been attributed to differences in the IHG protocol variables [12] including contraction intensity, frequency, time under tension (contraction duration), contraction to rest ratio and total exercise time [12,19], though, the effects of exercise different variables have not yet been investigated and understood.

Post-exercise hypotension (PEH), a phenomenon which occurs immediately after exercise is mainly due to a decreased vascular resistance in response to acute exercise [20] and it seems that PEH is related to IHG variables [12]. Determining the effects of IHG variables on hemodynamic and metabolic responses may help to find the most effective IHG protocol to achieve optimal exercise protocol for maximal reduction in BP. We hypothesized that higher repetitions (contraction frequency) and intensity of isometric exercise may cause greater reductions in blood pressure following exercise. Therefore, the present study was designed to determine the hemodynamic responses to five IHG protocols of different contraction intensity, duration, frequency, and contraction to rest ratio but similar workloads.

2. Methods

2.1. Participants

Fifteen sedentary men (mean \pm SD, age, 46 ± 6 years; 172 ± 6 cm and body mass, 89 ± 28 kg) with pre to stage 1 hypertension (SBP, 138 ± 7 mmHg; DBP, 89 ± 6 mmHg) volunteered to participate in this randomized controlled crossover study. All participants were free of any chronic disease and no one was taking any medication that could influence BP or other hemodynamic parameters. They did not have any regular physical training for at least 6 months prior to the study. Exclusion criteria included: smoking, drug therapy, chronic diseases and muscular or joint conditions that stop them from performing handgrip exercise. After screening for cardiovascular health by physician and explaining the study procedures, they completed an informed consent. The study procedure was approved by University Research and Ethics Committees (IR.SBU.ICBS.97.1024). This research was performed in compliance with the 1964 Helsinki Declaration.

2.2. Experimental design and exercise protocols

Forty-eight hours after familiarization session (visit 1), which was designed to familiarize the subjects with study procedures and IHG protocol, participants completed five IHG protocols in a random order on five separate sessions with 72 hours intervening (visits 2 to 6). Subjects were asked to refrain from performing any heavy activities and consuming any food or beverages containing caffeine at least 24 hours before each exercise trial. In order to avoid the effect of diet and sleep on the study results, subjects were asked to record the food consumed on the day before the test, to not consume any food 3 hours prior to the test and to have enough sleep at the night before the test. All sessions were carried out at the same time of the day (between 8:00 to 11:00 am) and at the laboratory temperature $24 \pm 2^\circ\text{C}$.

In each exercise trial, participants had 15 minutes rest in a seated position on an armchair, thereafter their resting BP and heart rate were measured, and a blood sample was taken for measuring plasma lactate. After baseline measurements, they performed one of the IHG protocols randomly by using a single-block design. The second blood sample was taken immediately after completing the exercise protocol. In addition, HR and BP were measured at 0, 5, 10,

15, 30, 45 and 60 minutes after exercise (during recovery). All IHG protocols were performed by using a digital hand dynamometer (DHD-3 Digital Hand Dynamometer, Saehan Corp, South Korea). Participants carried out 5 IHG protocols (including control session) with their non-dominant hand in the seated position, placing their forearm on the table to protect their elbow and flexed at 90° . At the beginning of each protocol, the participants carried out 3 maximal contractions without Valsalva maneuver, each separated by 30 s rest. The highest recorded trial was considered as the MVC [21,22]. The five IHG protocols included:

- high intensity high frequency (HIHF) protocol: 8×30 s isometric contractions at 60% of MVC, separated by 2 minutes rest;
- high intensity low frequency (HILF) protocol: 4×1 min isometric contractions at 60% of MVC, separated by 4 minutes rest;
- low intensity high frequency (LIHF): 8×1 min isometric contractions at 30% of MVC, separated by 2 minutes rest;
- low intensity low frequency (LILF) protocol: 4×2 min isometric contractions at 30% of MVC, separated by 4 minutes rest and;
- sham: 8×1 min isometric contractions at 3% of MVC, separated by 2 minutes rest.

Except for the sham, the workload for all exercise protocols were similar. All participants performed all protocols with the same dynamometer. The handgrip device displayed the data during contractions for each participant. All exercise trials were conducted in Exercise Physiology laboratory and under direct supervision of researcher. In all sessions, immediately after the completion of each protocol, rating of perceived exertion was also determined by using Borg scale of 6 to 20.

2.3. Hemodynamic and lactate measurements

After 15 minutes rest in the seated position, baseline values of SBP, DBP and HR were recorded. In order to evaluate the PEH response after each IHG protocol, BP and HR were measured at 0, 5, 10, 15, 30, 45, and 60 minutes of recovery. All measurements were taken on the dominant arm and at the brachial artery with an automated noninvasive BP monitor (Omron M6 Comfort, HEM-7221-E, Omron Healthcare, Kyoto, Japan) according to the guidelines presented by the American Heart Association [23]. The mean arterial pressure (MAP) was evaluated by using the following equation: $\text{MAP} = \text{DBP} + 1/3 (\text{SBP} - \text{DBP})$. Rate Pressure Product (RPP) was calculated according to the following equation: $\text{RPP} = \text{HR} \times \text{SBP}$ (bpm/mmHg).

Blood samples were collected from an antecubital vein in seated position at rest and immediately after the completion of each IHG protocol. The blood was transferred to an EDTA-containing tube and mixed thoroughly. Blood Samples were centrifuged at 3500 rpm for 10 minutes at 4°C and plasma samples were separated and stored at -80°C for further analyses. At the end of study, plasma samples were used to measure lactate concentration by using an auto-analyzer (Biosystems S.A., Barcelona, Spain).

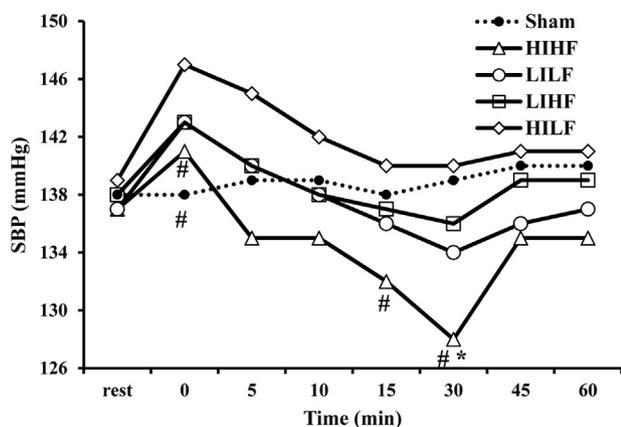


Figure 1 Mean values for SBP at baseline and during recovery following isometric handgrip interventions. * indicates a significant difference with sham and # shows a significant difference with HILF.

2.4. Statistical analyses

All data were collected and analyzed using the statistical package for the social science (SPSS version 22.0). The distribution of data was assessed by using the Shapiro-Wilk test. To compare the RPE and baseline values for BP, HR, plasma lactate and MVC in all trials, one-way repeated measures of Anova was employed. Two-way analyses of variance (Anova) with repeated measures were used to compare the HR, SBP, DBP, MAP and RPP (5 IHG \times 8 times) and plasma lactate (5 IHG \times 2 times) responses to the IHG trials. When Anova showed significant differences, post-hoc analyses were carried out using Bonferroni's test. Pearson's correlation was used to determine the relationship between plasma lactate and BP responses to IHGs. The level of significance was set at $P < 0.05$ for all statistical analyses. All data are presented as mean \pm standard deviation.

3. Results

All participants were able to complete all IHG protocols. There were no significant differences among baseline values for MVC, HR and BP ($P > 0.05$) in all trials. The RPE was significantly higher in all protocols compared to sham ($P < 0.01$), and that it was higher in HILF protocol than the other IHG protocols ($P < 0.01$).

Data analyses revealed a significant interaction (session \times time) for SBP ($P < 0.01$). Post-hoc analyses showed that SBP was significantly ($P < 0.01$) greater in response to HILF protocol (147 ± 7 mmHg) compared to HIHF (141 ± 9 mmHg) and sham (138 ± 7 mmHg) protocols (Fig. 1). During recovery, a significant PEH was observed for all trials irrespective of the trial type ($P < 0.05$). However, this PEH was greater following HIHF compared to HILF (12 mmHg more) and sham (11 mmHg more) at 30 minutes. The PEH for HIHF was also greater by 8 mmHg compared to HILF at 15 minutes during recovery.

Repeated measures of Anova showed a significant interaction for MAP ($P < 0.01$). MAP responses to HILF protocol were significantly ($P < 0.01$) higher than LIHF and sham (Fig. 2). During recovery (15 minutes), MAP for HIHF

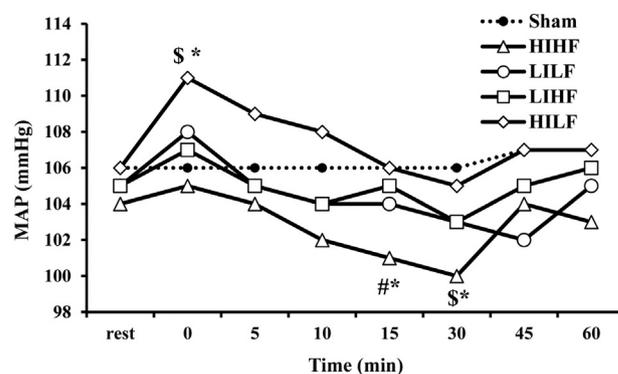


Figure 2 Mean values for MAP at baseline and during recovery following isometric handgrip interventions. * indicates a significant difference with sham, # shows a significant difference with HILF and \$ shows a significant difference with LIHF.

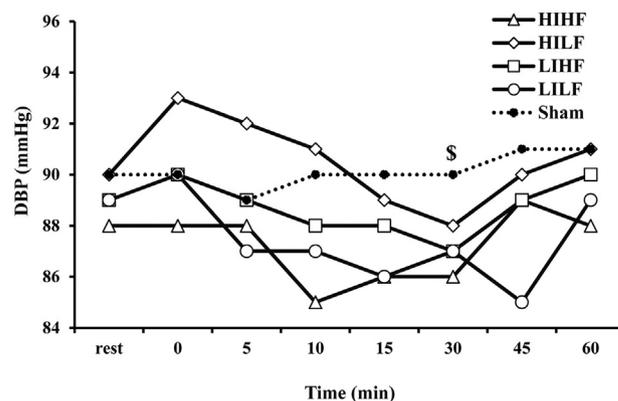


Figure 3 Mean values for DBP at baseline and during recovery following isometric handgrip interventions. \$ shows a significant difference with LIHF.

protocol showed a significant difference ($\Delta = -5$ mmHg) compared to HILF and sham ($P < 0.01$). However, MAP for the HIHF protocol was significantly ($P < 0.01$) lower than LIHF ($\Delta = -3$ mmHg) and sham ($\Delta = -6$ mmHg) protocols at 30 minutes.

Significant interaction was found for DBP ($P < 0.01$). Post-hoc analyses showed no significant ($P > 0.05$) effect of exercise on DBP (Fig. 3); though, DBP was only reduced significantly ($P < 0.01$) during recovery (30 minutes) in LIHF protocol compared to sham ($\Delta = -3$ mmHg). Responses of HR to HILF protocol were significantly ($P < 0.01$) lower than LIHF protocol (Fig. 4). At 45 minutes post-exercise, HR in HILF protocol was significantly ($P < 0.01$) different ($\Delta = -4$ bpm) than LIHF and sham.

In addition, RPP responses to exercise was significantly higher in LIHF protocol compared to sham ($P < 0.01$). However, at 30 minutes after exercise RPP for HIHF protocol was significantly ($P < 0.01$) less than LIHF and sham (Fig. 5).

Plasma lactate levels at rest and immediately after isometric exercise are depicted in Fig. 6. There were no significant differences among the resting values of lactate in all trials ($P > 0.05$). Significant ($P < 0.01$) interaction (session \times time) was observed for plasma lactate. In comparison to the sham trial (1.96 ± 0.6 mmol/L⁻¹) lactate values were significantly ($P < 0.05$) increased following HIHF (3.92 ± 1 mmol/L⁻¹), HILF (3.99 ± 0.98 mmol/L⁻¹), LIHF

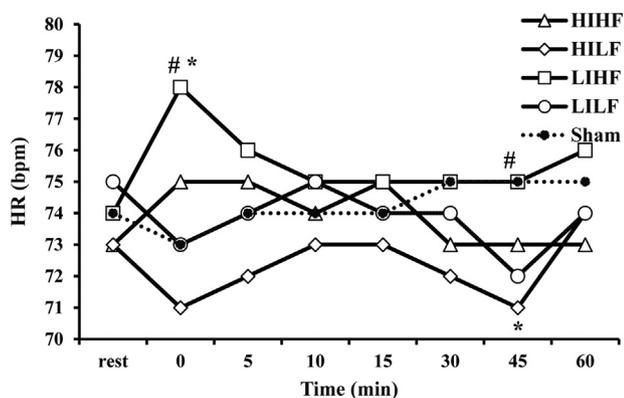


Figure 4 Mean values for HR at baseline and during recovery following isometric handgrip interventions. * indicates a significant difference with sham and # shows a significant difference with HILF.

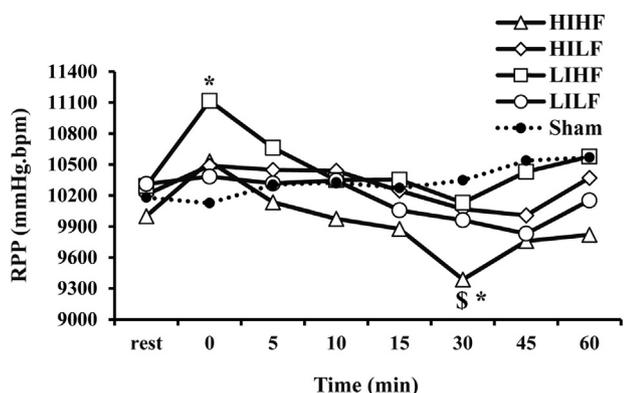


Figure 5 Mean values for RPP at baseline and during recovery following isometric handgrip interventions. * indicates a significant difference with sham and \$ shows a significant difference with LIHF.

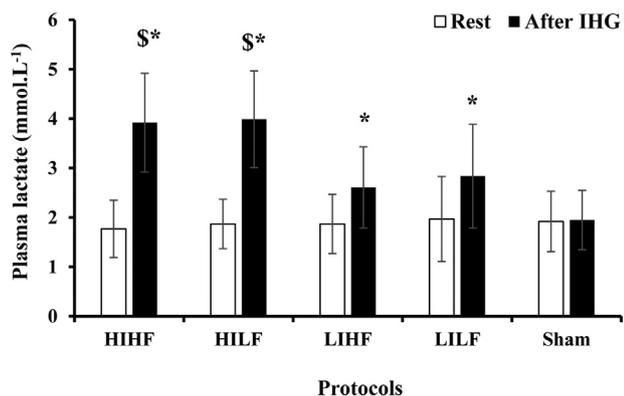


Figure 6 Plasma lactate levels (Mean ± SD) at rest and immediately after IHG. * Significant difference with Sham and § significant difference with the LIHF protocol.

($2.61 \pm 0.82 \text{ mmol/L}^{-1}$) and LILF ($2.84 \pm 1.05 \text{ mmol/L}^{-1}$) protocols. Meanwhile, lactate contraction was significantly higher in HIHF ($P < 0.05$) and HILF ($P < 0.01$) protocols compared to LIHF protocol. However, there was no significant ($P > 0.05$) correlation between responses of plasma lactate and SBP to isometric exercise (Fig. 6).

4. Discussion

The main finding of the present study is that responses of hemodynamic parameters to different IHG protocols similar workloads are different and affected by the frequency and duration of contractions, though, the metabolic responses are influenced by the intensity of exercise.

There are only two studies investigated the effects of different IHG protocols in hypertensive patients [12,13]. In the present study increases in SBP immediately following different IHG protocols, especially after HILF protocol compared to HIHF and sham, supports findings of Millar et al. (2011), who reported that in exercise protocols of similar intensities (30% of MVC) the protocol with higher contraction duration (2 minutes) induced the largest modulations in HR and SBP responses [12]. They concluded that increases in HR and BP to acute IHG are also mediated by contraction intensity as well as contraction and/or rest period-frequency-duration relationships [12].

In our study, it seems that HILF isometric protocol (high contraction intensity in combination with longer duration) induces higher SBP compared to HIHF. Since the contraction intensity in HIHF and HILF protocols is similar (60% of MVC) and despite the differences in total exercise duration, the contraction frequency and duration seems to be the main reason for higher hemodynamic changes following HILF protocol. In line with this, Olher et al. (2013) have reported no changes in hemodynamic parameters after two acute IHG protocols with very short (10 seconds) duration of contraction at 30% and 50% of MVC [13], while in the present study the contraction duration was in the range of 30 seconds to 2 minutes. Overall, our study confirms that at a similar contraction intensity, responses of SBP to IHG protocols are dependent on the frequency and contraction duration (time under tension).

Increases in HR after LIHF protocol compared to HILF shows that the contraction and rest period-frequency is probably more important than the contraction intensity for HR responses to IHG exercise. The increases in heart rate following LIHF protocol led to a significant increase in RPP following LIHF in comparison with sham.

Nevertheless, in the present study, increases in plasma lactate concentration following IHG protocols as a result of increases in intramuscular pressure, decreases in active skeletal muscle blood flow and increases in anaerobic activity [24], appears to be dependent on the contraction intensity. In HIHF and HILF trials, the contraction intensity was similar (60% MVC) and there was no significant difference in plasma lactate concentration between these protocols. However, lactate levels following LIHF (at 30% of MVC) were significantly lower than HIHF and HILF protocols. These findings confirm that plasma lactate responses are mostly dependent on the intensity of IHG and that changes in hemodynamic variables are not dependent on IHG-induced increases in plasma lactate. The latter was confirmed by lack of statistical correlation between plasma lactate and SBP in the present study.

In regard to the safety of IHG protocol [25], our study in accordance with others [12–15], showed no abnormality in all hemodynamic responses following IHG in male individuals with pre to stage one hypertension, because all

parameters returned to baseline values during 10 minutes recovery after the IHG. Therefore, it could be concluded that IHG with higher intensity (60% of MVC) and shorter contraction appears to be safe for these individuals.

4.1. Hemodynamic recovery from IHG protocols

Reduction in BP even as much as 5 mmHg can reduce the risk of stroke mortality by 14% and coronary heart disease by 9%, which is a valuable achievement [26]. It is likely that short-term responses after acute isometric exercise play an important role in BP adaptations to isometric exercise training [27].

In agreement with previous studies [12,15,17,28], in the present study, the magnitude of SBP reduction after 30 minutes of recovery compared to baseline was -9 mmHg in HIHF protocol, whereas reductions in SBP after 15 and 30 minutes of recovery in HIHF protocol compared to HILF protocol were higher nearly by -8 mmHg and -12 mmHg, respectively. These findings are in contrast with those of Millar et al. (2011) who reported similar SBP responses over the 30 minutes of recovery after three IHG protocols of similar intensities (30% of MVC) [12]. These contradictions might be related to the intensity of IHG, because in our study the intensity, duration and frequency were manipulated to equalize the IHG workload and we employed two different intensities (30 and 60% of MVC), whereas in Millar et al. (2011) IHG intensity was (30% of MVC) for all trails. The magnitude of SBP reduction in the study by Millar et al. [12], was less (-2 to -3 mmHg) than present study (-9 mmHg) that might be attributed to:

- higher baseline SBP value in our study (138 ± 7 mmHg) than the study by Millar et al. (122 ± 10 mmHg), because there is a direct association between PEH and baseline BP, the higher the baseline level, the greater the magnitude of PEH [29] and;
- the intensity of contraction which was twice more in present study (60% of MVC) than the study by Millar et al. (30% of MVC).

It has been suggested that changes in lactate concentration are associated with an increase in the intensity of the isometric handgrip contraction are related to the post-exercise hyperemia [30]. In addition, some studies have demonstrated that the magnitude and rate (i.e. speed) of BP reduction are greater with higher exercise intensity [31,32]. However, despite the high intensity of HILF protocol, it seems that the longer contraction duration has led to an increase in all hemodynamic parameters (except for HR at 45 minutes recovery) even during the recovery period in this protocol.

Similarly, MAP in HIHF protocol had a notable decrease at 15 minutes of recovery (-5 mmHg) compared to HILF and sham, and at 30 minutes of recovery in comparison with LIHF (-3 mmHg) and sham (-6 mmHg). Interestingly, DBP was only lower during recovery in LIHF protocol compared to sham (-3 mmHg).

Although the contraction to rest ratio was similar (1 to 4) for HIHF and HILF protocols, the contraction duration was twice more in HILF (1 minute) than HIHF (30 seconds) which

was compensated for by higher frequency in this protocol. In addition, rest period-frequency, and duration in HIHF were more than HILF in total (7×2 min vs 3×4 min). This may suggest that changes in SBP during recovery is mediated by contraction duration and frequency and are independent of contraction to rest ratio and total exercise time.

In fact, isometric exercise increases sympathetic responses via stimulation of neural reflexes associated with repeated contractions and local ischemia [33,34]. It seems that higher intensity of contraction in combination with higher contraction frequency in HIHF protocol, compared to other protocols, may have led to increases in mechanical contraction of the muscles, higher occlusion of blood flow to active muscles, increases in lactate concentrations and consequently increases in shear stress which in turn cause nitric oxide synthesis and vasodilation [35].

5. Conclusion

In summary, the findings of present study suggest that responses and recovery of hemodynamic parameters especially SBP depend on contraction frequency and duration (time under tension) in IHG exercise, and are independent of contraction to rest ratio and total exercise time. In addition, we detected that the metabolic responses to IHG are intensity related. Acute IHG exercise at 60% of MVC with shorter contraction and higher frequency is safe and can induce PEH during recovery in patients with pre to stage one hypertension. However, this information requires more investigation for better clinical implication.

Disclosure of interest

The authors declare that they have no competing interest.

Acknowledgments

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References

- [1] Organization WH. Global status report on noncommunicable diseases 2010. Geneva: World Health Organization; 2011.
- [2] Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Himmelfarb CD, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018;71(19):e127–248.
- [3] Pescatello LS, MacDonald HV, Lamberti L, Johnson BT. Exercise for hypertension: a prescription update integrating existing recommendations with emerging research. *Curr Hypertens Rep* 2015;17(11):87.
- [4] Churilla JR, Ford ES. Comparing physical activity patterns of hypertensive and nonhypertensive US adults. *Am J Hypertens* 2010;23(9):987–93.
- [5] Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. *J Am Heart Assoc* 2013;2(1):e004473.

- [6] Carlson DJ, Dieberg G, Hess NC, Millar PJ, Smart NA. Isometric exercise training for blood pressure management: a systematic review and meta-analysis. *Mayo Clinic Proceedings*. Elsevier; 2014.
- [7] Inder JD, Carlson DJ, Dieberg G, McFarlane JR, Hess NC, Smart NA. Isometric exercise training for blood pressure management: a systematic review and meta-analysis to optimize benefit. *Hypertens Res* 2016;39(2):88.
- [8] Jin YZ, Yan S, Yuan WX. Effect of isometric handgrip training on resting blood pressure in adults: a meta-analysis of randomized controlled trials; 2017.
- [9] Ash GI, Taylor BA, Thompson PD, MacDonald HV, Lamberti L, Chen M-H, et al. The antihypertensive effects of aerobic versus isometric handgrip resistance exercise. *J Hypertens* 2017;35(2):291.
- [10] da Silva CA, Mortatti A, Silva RP, Silva GB, Erberelli VFT, Stefanini F, et al. Acute effect of isometric resistance exercise on blood pressure of normotensive healthy subjects. *Int J Cardiol* 2013;168(3):2883–6.
- [11] Goessler K, Buys R, Cornelissen VA. Low-intensity isometric handgrip exercise has no transient effect on blood pressure in patients with coronary artery disease. *J Am Soc Hypertens* 2016;10(8):633–9.
- [12] Millar P, MacDonald M, McCartney N. Effects of isometric handgrip protocol on blood pressure and neurocardiac modulation. *Int J Sports Med* 2011;32(3):174–80.
- [13] Olher RdRV, Bocalini DS, Bacurau RF, Rodriguez D, Figueira Jr A, Pontes Jr FL, et al. Isometric handgrip does not elicit cardiovascular overload or post-exercise hypotension in hypertensive older women. *Clin Interv Aging* 2013;8:649.
- [14] Silva GO, Farah BQ, Germano-Soares AH, Andrade-Lima A, Santana FS, Rodrigues SL, et al. Acute blood pressure responses after different isometric handgrip protocols in hypertensive patients. *Clinics* 2018;73:e373.
- [15] Souza LR, Vicente JB, Melo GR, Moraes VC, Olher RR, Sousa IC, et al. Acute hypotension after moderate-intensity handgrip exercise in hypertensive elderly people. *J Strength Cond Res* 2018;32(10):2971–7.
- [16] Brook RD, Appel LJ, Rubenfire M, Ogedegbe G, Bisognano JD, Elliott WJ, et al. Beyond medications and diet: alternative approaches to lowering blood pressure: a scientific statement from the American Heart Association. *Hypertension* 2013;61(6):1360–83 [0b013e318293645f].
- [17] Van Assche T, Buys R, De Jaeger M, Coeckelberghs E, Cornelissen VA. One single bout of low-intensity isometric handgrip exercise reduces blood pressure in healthy pre-and hypertensive individuals. *J Sports Medicine Phys Fitness* 2017;57(4):469.
- [18] Peters PG, Alessio HM, Hagerman AE, Ashton T, Nagy S, Wiley RL. Short-term isometric exercise reduces systolic blood pressure in hypertensive adults: possible role of reactive oxygen species. *Int J Cardiol* 2006;110(2):199–205.
- [19] Galvez JM, Alonso JP, Sangrador LA, Navarro G. Effect of muscle mass and intensity of isometric contraction on heart rate. *J Appl Physiol* 2000;88(2):487–92.
- [20] MacDonald JR. Potential causes, mechanisms, and implications of post exercise hypotension. *J Hum Hypertensi* 2002;16(4):225.
- [21] Frederiksen H, Hjelmborg J, Mortensen J, Mccue M, Vaupel JW, Christensen K. Age trajectories of grip strength: cross-sectional and longitudinal data among 8,342 Danes aged 46 to 102. *Ann Epidemiol* 2006;16(7):554–62.
- [22] Crosby CA, Wehbe MA. Hand strength: normative values. *J Hand Surg* 1994;19(4):665–70.
- [23] Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, et al. Recommendations for blood pressure measurement in humans and experimental animals: part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. *Circulation* 2005;111(5):697–716.
- [24] Barcroft H, Millen J. The blood flow through muscle during sustained contraction. *J Physiol* 1939;97(1):17–31.
- [25] Kraemer WJ, Adams K, Cafarelli E, Dudley GA, Dooly C, Feigenbaum MS, et al. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 2002;34(2):364–80.
- [26] Stamler R. Implications of the INTERSALT study. *Hypertension* 1991;17(1):116.
- [27] Hecksteden A, Grütters T, Meyer T. Association between postexercise hypotension and long-term training-induced blood pressure reduction: a pilot study. *Clin J Sport Med* 2013;23(1):58–63.
- [28] Millar PJ, MacDonald MJ, Bray SR, McCartney N. Isometric handgrip exercise improves acute neurocardiac regulation. *Eur J Appl Physiol* 2009;107(5):509.
- [29] Moraes M, Bacurau RFP, Simões H, Campbell C, Pudo M, Wasinski F, et al. Effect of 12 weeks of resistance exercise on post-exercise hypotension in stage 1 hypertensive individuals. *J Hum Hypertens* 2012;26(9):533.
- [30] Devereux GR, Coleman D, Wiles JD, Swaine I. Lactate accumulation following isometric exercise training and its relationship with reduced resting blood pressure. *J Sports Sci* 2012;30(11):1141–8.
- [31] Wiles JD, Coleman DA, Swaine IL. The effects of performing isometric training at two exercise intensities in healthy young males. *J Appl Physiol* 2010;108(3):419–28.
- [32] Baross AW, Wiles JD, Swaine IL. Effects of the intensity of leg isometric training on the vasculature of trained and untrained limbs and resting blood pressure in middle-aged men. *Int J Vasc Med* 2012;2012:964697.
- [33] Taylor AC, McCartney N, Kamath MV, Wiley RL. Isometric training lowers resting blood pressure and modulates autonomic control. *Med Sci Sports Exerc* 2003;35(2):251–6.
- [34] Millar P, Levy A, McGowan C, McCartney N, MacDonald M. Isometric handgrip training lowers blood pressure and increases heart rate complexity in medicated hypertensive patients. *Scand J Med Sci Sports* 2013;23(5):620–6.
- [35] Clifford PS, Hellsten Y. Vasodilatory mechanisms in contracting skeletal muscle. *J Appl Physiol* 2004;97(1):393–403.