

[ORIGINAL ARTICLE]

Effects of Isometric Handgrip Training on Home Blood Pressure Measurements in Hypertensive Patients: A Randomized Crossover Study

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Abstract:

Objective We aimed to examine the effects of isometric handgrip (IHG) training on home blood pressure (BP) levels in hypertensive Japanese patients undergoing treatment.

Methods Fifty-three hypertensive patients (mean age, 61.7 years; 56.6% men) with a home systolic BP \geq 135 mmHg and/or a home diastolic BP \geq 85 mmHg were randomly assigned to either group A or B. As per the crossover design, group A performed 8 weeks of IHG training, followed by an equivalent training-free, control period, while the reverse protocol was performed by group B. The baseline characteristics were similar between both groups. The individualized daily IHG training comprised four sets of 2-min isometric contractions at 30% of the individual's maximum voluntary contraction capacity, including 1 min of rest between sets, for \geq 3 days/week. The outcome measure was morning and evening home BP readings taken over the last 2 weeks of the training and control periods.

Results A combined data analysis for both groups showed that IHG training was significantly associated with the lowering of both systolic and diastolic BP in the morning (137.9 \pm 9.3 vs. 135.3 \pm 9.5 mmHg, $p=0.007$ and 83.0 \pm 9.5 vs. 81.2 \pm 9.3 mmHg, $p<0.001$, respectively) and evening (130.0 \pm 10.7 vs. 127.6 \pm 10.1 mmHg, $p=0.003$ and 75.8 \pm 10.4 vs. 73.8 \pm 9.2 mmHg, $p<0.001$, respectively), while no significant change was observed after the control period. A larger increase in the maximum grip strength due to IHG training was associated with greater BP reductions.

Conclusion An 8-week period of IHG training significantly lowered both the morning and evening home BP in hypertensive Japanese patients undergoing treatment.

Key words: home blood pressure, isometric handgrip training, hypertension, non-pharmacological treatment, grip strength

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Introduction

Hypertension is a leading cause of cerebrovascular and cardiovascular diseases (1, 2). Non-pharmacological treatments, such as a reduction of both salt and alcohol consumption, smoking cessation, and increase in physical activity, constitute basic preventive strategies that should be prac-

ticed by all hypertensive patients (3-5). Following a daily regimen of moderate aerobic exercise for \geq 30 min is also recommended for hypertension treatment (6). A meta-analysis demonstrated that simple resistance training or isometric handgrip (IHG) training could significantly decrease blood pressure (BP) (7). IHG training is very practical because it does not require any special space or expensive equipment (8). This indoor exercise modality, unlike jogging

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or walking, is not limited by weather conditions. Additionally, the training is feasible for individuals who report difficulty in exercising either due to limited space, time constraints, or concurrent physical impairments, such as lower limb disability. Moreover, the Prospective Urban Rural Epidemiology (PURE) study (9) reported higher handgrip strength as an independent predictor for cardiovascular diseases, suggesting that IHG training might have favorable cardiovascular effects other than BP control.

The effects of IHG training on BP have been examined in different populations, including hypertensive (10-12) and normotensive (8, 13) subjects, who demonstrated a significant decrease in BP following IHG training. However, the studies used BP values evaluated at a clinic as outcome measures. Moreover, most of the subjects were Caucasian, with only a few studies including Asians. The etiology of hypertension among Asians differs significantly from that in Caucasians owing to genetics (14, 15) and lifestyles (16). To our knowledge, only one study has previously examined the effects of IHG training in untreated, hypertensive Japanese patients, and the study found that both brachial and central BP decreased significantly after 8 weeks of training (17). Although this result suggests that IHG training may lead to BP reduction in Asian subjects, more evidence of the beneficial effects of IHG training in this population is required. To the best of our knowledge, the effects of this exercise modality on home BP values have not yet been reported.

Using a randomized crossover study, we aimed to investigate our hypothesis that IHG training may significantly reduce home BP values in hypertensive Japanese patients. Home BP measurements are known to correlate with end organ damage in hypertensive patients and are considered better markers for predicting the risk of cardiovascular events than clinic BP values (6, 18-20). We believe that if it is verified that IHG training reduces home BP measurements, the finding would validate the clinical and practical utility of this simple exercise modality.

Materials and Methods

Study design and patients

In this multicenter crossover study, we included outpatients who visited the clinics of Tohoku, Fukushima, and Aomori Rosai hospitals. The study was conducted in compliance with the Helsinki declaration for the study of human subjects and was registered in the UMIN Clinical Trial Registry (No. 000035866). The institutional review board of Tohoku Rosai Hospital approved the study protocol, and all study participants provided their written informed consent prior to study participation.

We recruited hypertensive patients who routinely monitored and recorded their BP at home. Patients with a mean systolic BP of ≥ 135 mmHg and/or those with a mean diastolic BP of ≥ 85 mmHg, measured in the morning over 5 days, met the study's eligibility criteria. The exclusion criteria

were: 1) clinic BP measurement of $\geq 180/110$ mmHg, 2) history of cerebrovascular or cardiovascular events within the previous 6 months, 3) concurrent chronic kidney disease of stage G3b or lower (21), 4) ongoing cancer treatment, and 5) ongoing hormone replacement therapy. Finally, 53 eligible patients (56.6% men, mean age = 61.7 years) were registered for the study. Height (cm) was measured manually using a height meter (BSM 370, InBody Japan, Tokyo, Japan). Abdominal circumference was measured at the level of the umbilicus at the end of expiration. Body weight and body mass index (BMI) were examined using a body composition analyzer (InBody 720, InBody Japan) (22).

In this prospective crossover study conducted over 16 weeks, the patients were first randomized into either group A or B using the envelope method. Fig. 1 shows the outline of the study. After the baseline assessment, group A patients performed IHG training for an 8-week period, which was followed by a similar length of training-free, control period. Conversely, group B patients underwent the training regimen in the latter 8 weeks, with an initial exercise-free 8-week period.

The IHG training protocol was determined according to previous reports (8, 10-13). During the baseline assessment, the maximum grip strengths of both hands were determined for each participant. The subjects were asked to hold a handgrip spring dynamometer (GRIP-D, TAKEI, Niigata, Japan) in the right hand using a full grip. The subject compressed the handles of the dynamometer with the application of maximum effort for a few seconds. After adequate rest, the maximum grip of the left hand was examined in a similar fashion. Two measurements of grip strength were obtained for each hand, and the mean of the maximum grip strength values for each hand was regarded as the maximal grip strength. The examination of maximum grip strength was repeated at the end of the first and second 8-week periods (Fig. 1).

The subjects were guided to perform IHG training at home or at their workplace using a suitable device (DIGI-FLEX, FEI). We prepared four kinds of spring handgrip training devices with different levels of resistance (light, 4.54 kg; medium, 7.26 kg; heavy, 10.43 kg; very heavy, 14.06 kg). Each subject was given a device whose resistance level was close to 30% of his/her maximal isometric contraction. The subjects were asked to perform four sets of isometric handgrip contractions in the standing position using each hand for a 2-min duration, with 1 min of rest between sets. The isometric exercise was to be performed at least 3 days a week for 8 weeks. During the control period, subjects were instructed to continue their routine lifestyle. Antihypertensive medications were not changed during the entire study period unless marked BP fluctuations were observed.

Measurement of home BP

The patients were asked to measure their BP at home every morning and evening at baseline and during the last 2

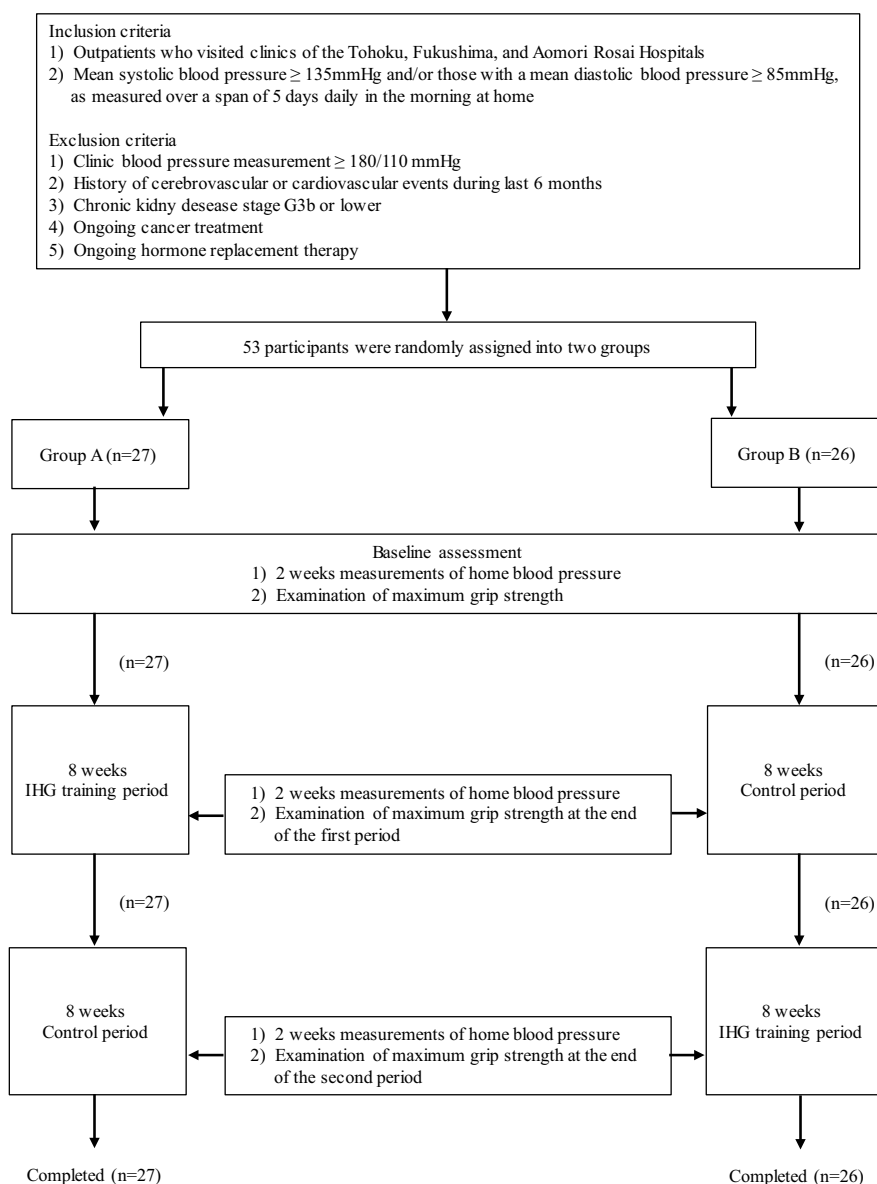


Figure 1. Flowchart of the study. All participants duly completed the study protocol. IHG training: isometric handgrip training

weeks of the first and second 8-week periods (Fig. 1). Validated oscillometric monitors (HEM-7080IT Omron Healthcare, Kyoto, Japan) were supplied to all participants for self-monitoring of BP. The subjects measured their BP after resting for ≥ 2 min in a sitting position, within 1 hour of waking up in the morning (before breakfast and prior to taking antihypertensive medications) and before going to bed in the evening, as outlined in the Japanese guidelines for the management of hypertension (23). Two measurements were obtained at each time, and the mean BP was used as the representative value.

Statistical analysis

All data are expressed as the mean \pm standard deviation (SD) or as percentages. Group comparisons were performed using the t-test and Chi-square test for continuous and categorical variables, respectively. Inter-group differences were

examined using the paired t-test. All statistical analyses were performed using the JMP (version 14.0 for Windows; SAS Institute, Cary, USA) software. A p value < 0.05 was considered to be statistically significant.

Results

A total of 40, 9, and 4 participants were recruited from Tohoku, Fukushima, and Aomori Rosai hospitals, respectively. Of these 53 participants, 27 and 26 participants were randomly assigned to groups A and B, respectively. Participants in both groups duly completed the outlined study protocol (Fig. 1). Table 1 shows the baseline characteristics of all participants. The groups did not differ significantly in age, sex, BMI, maximum isometric strength, baseline home BP, heart rate, and prescribed antihypertensive medications. The frequencies of comorbidities such as diabetes, dyslipide-

Table 1. Patient Characteristics.

Variables	Group A (n=27)	Group B (n=26)	p value
Age, years	62.3±11.7	61.2±13.3	0.748
Sex (male), %	51.9	61.5	0.477
Height, cm	163.5±10.2	163.2±10.9	0.911
BMI, kg/m ²	25.2±3.1	25.5±3.9	0.786
Waist circumference, cm	88.1±4.7	91.3±12.0	0.262
Maximum grip strength, kg	34.6±12.6	33.1±10.9	0.797
Morning HSBP, mmHg	136.9±8.2	141.0±11.1	0.129
Morning HDBP, mmHg	81.9±10.1	84.8±8.1	0.266
Morning HHR, bpm	66.8±9.5	67.2±8.1	0.860
Evening HSBP, mmHg	129.3±9.3	132.6±12.9	0.286
Evening HDBP, mmHg	75.4±10.7	77.0±9.5	0.574
Evening HHR, bpm	71.1±9.0	72.6±10.9	0.609
Diabetes, %	3.7	7.7	0.529
Dyslipidemia, %	37.0	26.9	0.430
Hyperuricemia, %	7.4	11.5	0.607
Medication for hypertension, %	74.1	76.9	0.810
Calcium channel blocker, %	51.9	61.5	0.477
Angiotensin II receptor blocker, %	48.2	65.4	0.206
Diuretic, %	25.9	23.1	0.810
β blocker, %	0.0	7.7	0.142
Others, %	14.8	15.4	0.954
Medication for diabetes, %	3.7	7.7	0.530
Medication for dyslipidemia, %	37.0	26.9	0.430

BMI: Body mass index, HSBP: home systolic blood pressure, HDBP: home diastolic blood pressure, HHR: home heart rate

Data are shown as mean±SD or percentage.

Table 2. Group-wise Changes in Home Blood Pressure and Maximum Grip Strength between Baseline and 16 Weeks.

Variables	Group A (n=27)			Group B (n=26)		
	Baseline	8 weeks	16 weeks	Baseline	8 weeks	16 weeks
Morning HSBP, mmHg	136.9±8.2	134.0±8.1*	133.0±7.3*	141.0±11.1	138.9±10.4	136.7±10.8*
Morning HDBP, mmHg	81.9±10.1	79.5±9.5**	79.7±9.0**	84.8±8.1	84.2±8.9	83.0±8.9
Morning HHR, bpm	66.8±9.5	68.2±9.6	68.2±8.7	67.2±8.1	68.5±8.0*	69.2±10.2
Evening HSBP, mmHg	129.3±9.3	126.7±9.8*	126.3±8.4	132.6±12.9	130.7±12.2	128.6±10.5**†
Evening HDBP, mmHg	75.4±10.7	73.1±9.9**	73.5±9.3*	77.0±9.5	76.2±10.2	74.6±8.5*†
Evening HHR, bpm	71.1±9.0	72.1±9.7	72.2±9.3	72.6±10.9	72.2±9.6	72.3±10.2
Maximum grip strength, kg	34.6±12.6	35.2±14.4	35.2±14.5	33.1±10.9	33.5±11.3	34.2±11.1*

HSBP: home systolic blood pressure, HDBP: home diastolic blood pressure, HHR: home heart rate

Data are shown as mean±SD or percentage.

*p<0.05 vs. baseline, **p<0.01 vs. baseline, †p<0.05 vs. 8 weeks.

mia, and hyperuricemia were also comparable between both study groups. None of the subjects required a change in antihypertensive medications throughout the study period.

Table 2 shows values for morning and evening BP, heart rate, and maximum grip strength at baseline and at 8 and 16 weeks for both groups. The period of intervention was the first 8 weeks for group A and the latter 8 weeks for group B. In group A, both systolic and diastolic BP were significantly lowered in the morning and evening during the 8 weeks of intervention (p<0.05 and p<0.001, respectively). A similar tendency was observed in group B, although the fall

in BP was not statistically significant. At 16 weeks, morning systolic BP (p<0.05) and both morning and evening diastolic BP (p<0.01 and p<0.05, respectively) were significantly lower than the baseline levels in group A. In group B, at 16 weeks, morning systolic BP (p<0.05) and evening systolic (p<0.01) and diastolic (p<0.05) BP readings were significantly lower than those at baseline. In addition, evening systolic and diastolic BP readings at 16 weeks were significantly lower than the values at 8 weeks (p<0.05 for both).

On a combined assessment of the data of both groups, IHG training was found to be significantly associated with a

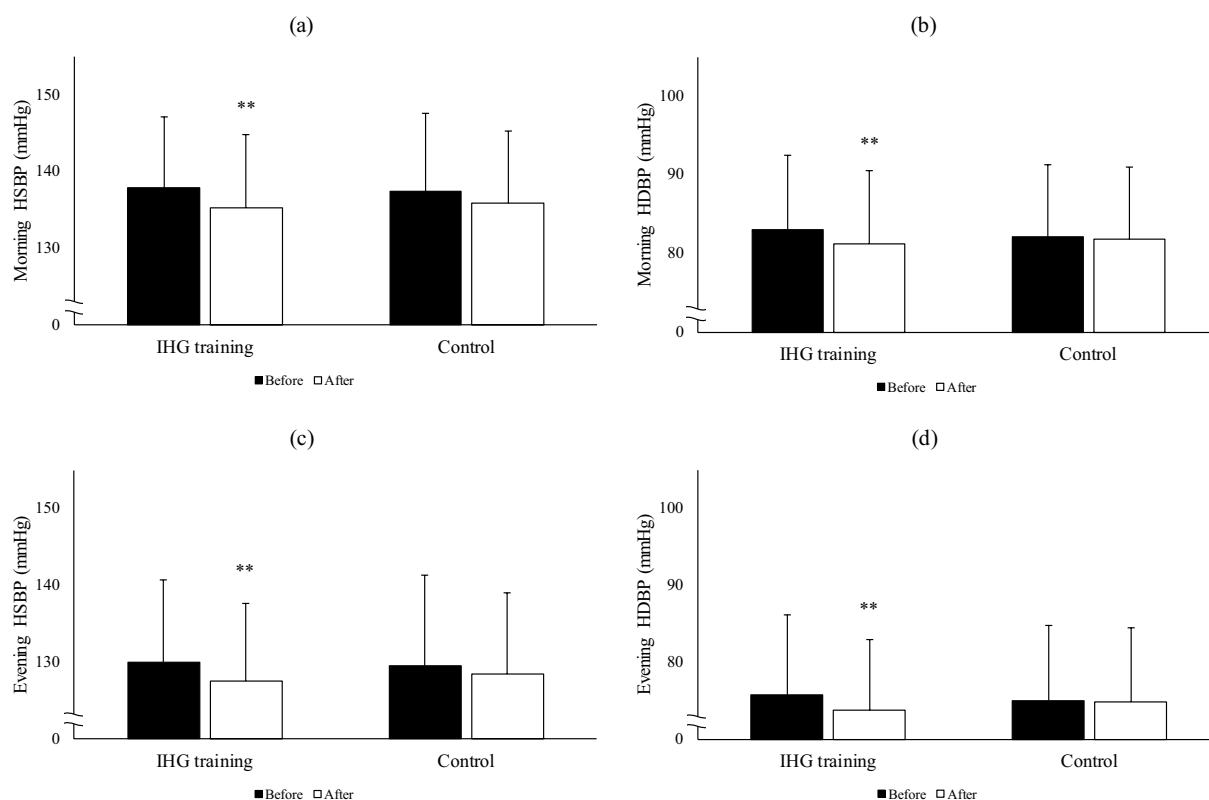


Figure 2. Changes in the home blood pressure values before and after the control and IHG training periods. Each figure shows (a) morning HSBP, (b) morning HDBP, (c) evening HSBP, (d) evening HDBP. IHG training: isometric handgrip training, HSBP: home systolic blood pressure, HDBP: home diastolic blood pressure. ** $p < 0.01$ vs. before.

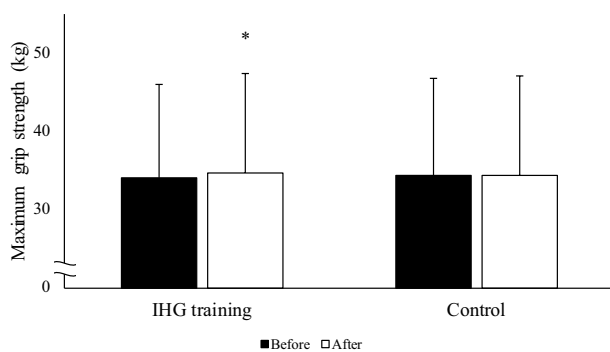


Figure 3. Changes in the maximum grip strength before and after the control and IHG training periods. IHG training: isometric handgrip training. * $p < 0.05$ vs. before.

reduction of both the systolic and diastolic BP in the morning (systolic, $p = 0.007$; diastolic, $p < 0.001$) and evening (systolic, $p = 0.003$; diastolic, $p < 0.001$ for diastolic), while no significant changes in BP were observed during the training-free control period (Fig. 2). The heart rate remained unchanged in the training and control periods. The maximum grip strength increased significantly during the exercise intervention, while no change in maximum grip strength was observed during the control period (Fig. 3).

To further confirm the link between the changes in grip strength and blood pressure reduction, we compared the hypotensive effects of IHG training according to the changes

in grip strength after the intervention (Fig. 4). The subjects were divided into two groups based on the changes in grip strength - an upper half and a lower half [IHG/Grip (U) and IHG/Grip (L), respectively]. The IHG/Grip (U) group showed a significant reduction in both morning and evening systolic and diastolic BPs compared to baseline, while the IHG/Grip (L) group showed a significant reduction in evening diastolic BP alone. We also performed a similar analysis using data collected just before and at the end of the control period. Again, the subjects were divided into two groups based on changes in grip strength - an upper [CON/Grip (U)] and a lower [CON/Grip (L)] half. There was no significant change in systolic or diastolic BP in the CON/Grip (U) and CON/Grip (L) groups, although the CON/Grip (U) group tended to show a greater BP reduction than the CON/Grip (L) group.

Discussion

We used a randomized crossover study design to examine the effects of IHG training on the resting BP in hypertensive Japanese patients undergoing treatment. The main outcome measure was the home BP level, which is superior to clinic-measured BP with respect to prognostic significance. We found that 8 weeks of IHG training significantly lowered both morning and evening BP. As shown in Table 2, the decreases in morning systolic and diastolic BP levels were 2.3

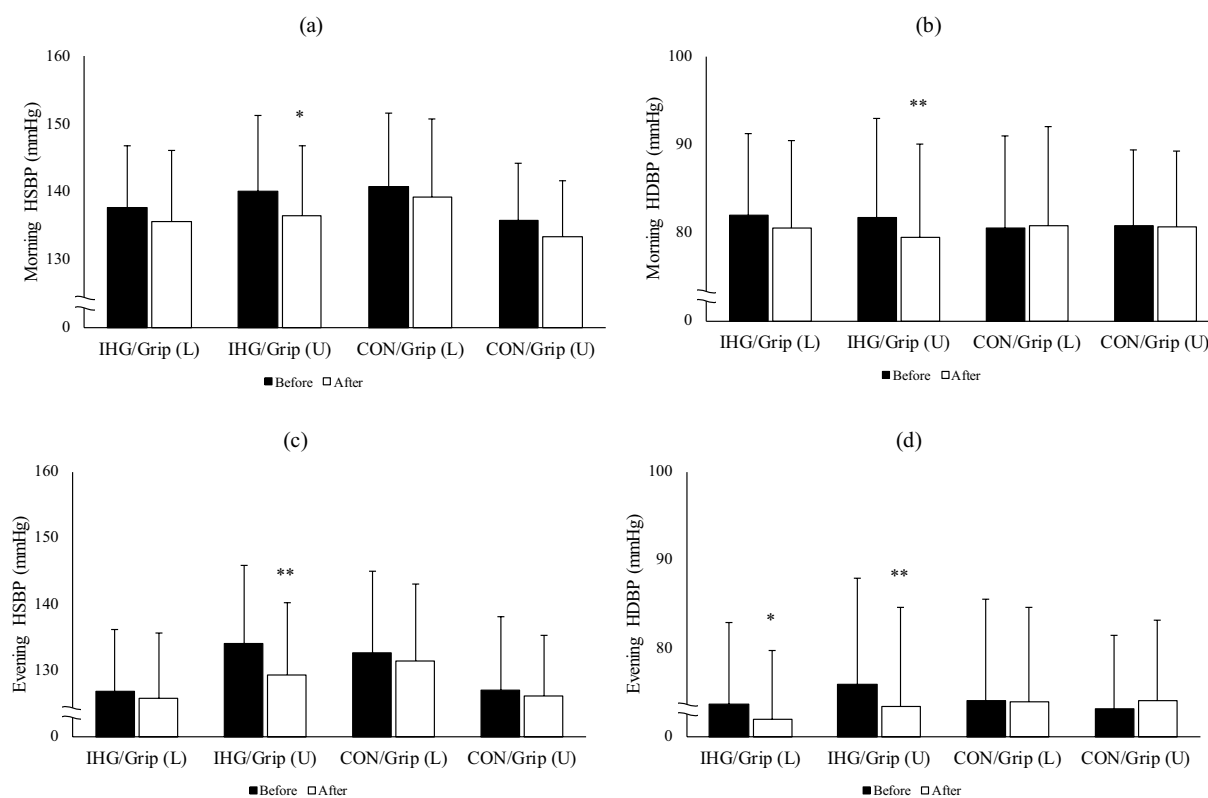


Figure 4. Changes in the home blood pressure values according to the lower or upper half increase in maximum grip strength during the control or IHG training period. Grip (L) and grip (U) indicate lower and upper half increase in grip strength during a given period. (a), (b), (c), and (d) represent morning HSBP, morning HDBP, evening HSBP, and evening HDBP, respectively. CON: control period of group B, IHG: isometric handgrip training period, HSBP: home systolic blood pressure, HDBP: home diastolic blood pressure. * $p < 0.05$ vs. before, ** $p < 0.01$ vs. before.

and 1.7 mmHg, respectively. Similarly, evening systolic and diastolic BP readings decreased by 2.1 and 1.8 mmHg, respectively. Our data are consistent with those of previous studies which applied similar exercise modalities and demonstrated an association between exercise and significantly decreased clinic BP readings in both Caucasian and Japanese hypertensive patients (10-12, 17). The Ohasama study showed that an increase in the mean home systolic (10 mmHg) and diastolic (5 mmHg) BP measurements over 2 weeks was associated with a 31% and 20% increase in the risk of stroke and transient ischemic attacks, respectively (20). The real-world, large-scale prospective, observational home blood pressure measurement with Olmesartan Naïve patients to establish standard target blood pressure (HONEST) study involving >20,000 hypertensive Japanese patients receiving treatment demonstrated that the risk of cardiovascular events was lowest in patients with morning, home systolic BP readings of ≤ 124 mmHg, while the risk significantly increased when the controlled clinic systolic BP values were ≥ 145 mmHg (24). These results highlight the importance of lowering morning home systolic BP to 124 mmHg, to minimize the risk of the occurrence of cardiovascular complications. In the present study, we used the mean home BP readings taken over 2 weeks as the outcome measure, and could therefore show the significant effects of

IHG training in achieving better BP control.

The mechanisms of BP reduction due to IHG training are not well understood although favorable effects on vascular function may be involved. It has been shown that 4-8 weeks of IHG training significantly improved endothelial function, assessed using flow-mediated dilation, in hypertensive patients (25) and in those with chronic heart failure (26, 27). A similar outcome was also observed in the elderly (28). Moreover, a similar exercise modality has been reported to significantly increase forearm blood flow in young and middle-aged populations (29), suggesting a mechanism of functional improvement in flow-mediated vasodilation.

As shown in Table 2, the BP reduction was slightly less in group B than in group A. This may have been due to the slightly lower pre-intervention BP levels (1.9-2.1 mmHg) in group B, which was possibly due to a possible placebo effect. Thus, the BP lowering effect of IHG training may have been underestimated in group B compared to group A. However, the BP values at 16 weeks were significantly lower than the values at baseline, even in group B patients (Table 2).

Moderate-intensity IHG exercise of up to 30% of the maximum voluntary muscle contraction capacity of the patient is reportedly safe because it is unlikely to increase cardiovascular risk by potentiating cardiac vagal activity, lead-

ing to an increased heart rate (10, 30). In our study, the heart rate remained unchanged after IHG training; a finding which corroborated with the results of previous studies. Moreover, none of the subjects quit the study, which suggested that they found the application of the exercise modality feasible.

The hypotensive effects of IHG training were not substantially different from the placebo effects, as shown in group B. To further confirm the link between grip strength changes induced by IHG and blood pressure reduction, we compared the hypotensive effects between IHG/Grip (U) and IHG/Grip (L). Fig. 4 shows that the IHG/Grip (U) group showed significantly greater hypotensive effects than the IHG/Grip (L) group. Moreover, there was no clear relationship between the changes in the maximum grip strength and the changes in blood pressure in the control period. Thus, our data suggests that the increase in grip strength due to IHG training is associated with larger BP reductions.

A recent review has also shown that, compared to muscle mass, muscle strength is more involved in the improvement of vascular function and/or the risk reduction associated with resistance training (31). Fahs et al. showed that muscle strength is inversely associated with arterial stiffness assessed using pulse wave velocity (32). Moreover, consistent with the findings of the present study, it has been shown that low-level resistance training significantly increased muscle strength, but not muscle mass (31). Understanding the mechanisms underlying the relationship between muscle strength and blood pressure regulation requires further investigation.

This study is associated with several limitations. First, because IHG training was conducted at home, and not under medical supervision, it is unclear how accurately and diligently the subjects adhered to the prescribed training regimen. However, the subjects received regular follow-up calls to discuss the training protocol and to confirm and improve the quality of practice. In addition, questions or difficulties related to the training were adequately resolved during the calls. Second, we did not collect any information on lifestyle factors, such as the regular diet. Participation in this clinical study might have encouraged some subjects to favorably modify their lifestyle, which could have contributed towards a decrease in BP. Third, we did not include a wash-out period between the intervention and exercise-free control periods. Therefore, the effect of IHG training might have been underestimated in group B compared to group A because the intervention period preceded the control period in group A. Therefore, BP measurement taken just before the initiation of IHG training might have been comparatively lower in group B due to a placebo effect exerted by the preceding 8-week control period. However, in group B, the morning systolic BP readings and both evening systolic and diastolic BP levels at 16 weeks were significantly lower than the values at baseline, despite a statistically non-significant BP reduction during the 8-week interval. This finding supports the notions that IHG training can reduce BP and IHG

training is superior to any possible placebo effect observed in group B.

In conclusion, this study showed that an 8-week IHG training period significantly lowered both morning and evening home BP levels in hypertensive Japanese patients receiving treatment. The IHG exercise modality can be widely applied in hypertensive patients because it is easy, safe, inexpensive, and does not have space specifications. Reduction in BP was associated with a significant increase in maximum grip strength. Mechanisms of how grip strength relates to blood pressure regulation needs further study.

The authors state that they have no Conflict of Interest (COI).

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