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Effects of isometric contraction training on hypertensive patients : A Systematic Review

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Abstract

Introduction:

Hypertension is one of the major threats to the health of the entire population in today's society. Poor blood pressure values represent health warnings and are also a risk factor for cardiovascular diseases such as stroke, heart disease, angina pectoris, and peripheral arterial disease. The National Cardiovascular Disease Center's "China Cardiovascular Health and Disease Report 2023" data shows that the prevalence of hypertension in adults has reached 31.6%, with a total of 245 million patients. Moreover, studies have shown that 43.1% of the population have normal high blood pressure, with an estimated number of 4.35. The same problem occurs not only in China, but also in the statistics of the Centers for Disease Control and Prevention in the United States. Nearly 47% of the American population has hypertension. Isometric contraction training is a type of resistance training that was often considered to be avoided by hypertensive patients in previous exercise guidance. However, in recent years,

research has shown that under appropriate control, it can effectively lower blood pressure. This study explores the effects of isometric contraction training on blood pressure during acute and non acute interventions by searching and organizing relevant literature, and attempts to find new strategies as non pharmacological treatments for hypertension. Based on past research, it has been found that long-term isometric contraction training has a consistent effect on lowering blood pressure. Although there are immediate changes in acute intervention studies, the duration is very short. The use of equal length contraction training or ischemic preconditioning as a non pharmacological blood pressure improvement strategy has been proven to be safe and effective, with high process controllability, and may be a more feasible strategy in the future.

Aim of the study:

This study aims to evaluate the relevant literature on equal length contraction training as a strategy for reducing blood pressure, explore the correlation between experimental methods and the degree of blood pressure reduction, and attempt to find more effective ways in non pharmacological treatment strategies for hypertension.

Material and methods:

After conducting a systematic search of the following databases, this article identified potentially qualified grey literature from Pubmed, Web of Science, and Google Scholar, as well as journals in related fields. There are no restrictions on language or publishing timeline. The retrieval strategy uses keywords, medical keywords (MeSH), and Boolean conjunctions, including isometric contract or tension, AND (Contract, Isometric or Contracts, Isometric or Isometric Contracts), and AND (Blood Pressure, High or Blood Pressures, High or High Blood Pressure or High Blood Pressures。 In addition, a literature review was conducted to further identify randomized controlled trials that met the inclusion criteria.

Conclusions:

IHG can significantly reduce SBP、DBP and MAP in hypertensive patients. Therefore, we recommend that this type of exercise (especially wall squatting and grip strength exercises) is considered an effective therapy for reducing arterial hypertension. The efficiency of this intervention is limited to the short term. Therefore, long-term effects (at least 1 year) should be studied.

Key words:hypertension; Systematic Review; Equal length contraction training

Introduction

The definition of hypertension is divided into four levels according to the "2017 Prevention Guidelines, Testing, Evaluation, and Management" published by the American College of Cardiology. Adult blood pressure is defined in each level as: normal blood pressure, with systolic blood pressure<120 mmHg and diastolic blood pressure<80mmHg; Elevated hypertension, with systolic blood pressure ranging from 120 to 129 mmHg and diastolic blood pressure<80 mmHg; Hypertension is further divided into two levels: Stage 1 refers to a systolic blood pressure between 130 and 139 mmHg or a diastolic blood pressure between 80 and 89 mmHg; Stage 2 hypertension is defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg. According to the seventh report of the National Joint Committee on the Prevention, Detection, Evaluation, and Treatment of Hypertension in the United States, hypertension is defined as systolic/diastolic blood pressure>140/90mmHg, and when it is between 120/80-140/90mmHg, it belongs to prehypertension.

In non pharmacological control of hypertension, the focus is on changing lifestyle. The American Heart Association [5] has proposed six non pharmacological treatment recommendations for hypertension: 1. Weight loss; 2、 A diet beneficial to heart health, such as the DASH diet [6], which includes sufficient intake of whole grains, fruits, vegetables, legumes, fat free or low-fat dairy products, and fish rich in Omega-3; 3、Limit sodium intake; 4、 Potassium supplements; 5、 Increase physical activity and planned exercise in daily life; 6、 Restrictions on alcohol consumption. I also hope to gradually develop it into five ideal lifestyle habits: healthy diet, weight loss, moderate exercise, non-smoking (quitting smoking), and limited alcohol consumption. Among these six non pharmacological treatment recommendations, exercise is the most proactive approach, and this viewpoint has received a lot of support in recent research reports. In a retrospective study, it was found that hypertensive patients with and without exercise habits had an average 30-50% lower risk of developing hypertension compared to the latter, and there were no differences in age, race, or gender [7].

Mughal et al. (2001) found that any form of aerobic exercise can achieve the effect of improving blood pressure [8]. The American Heart Association (AHA) and the American College of Cardiology (ACC) published their "Life Guidelines for Reducing Cardiovascular Risk" in 2014, which stated that aerobic exercise can consistently reduce low-density lipoprotein (LDL-C) levels by 3-6 mg dL-1, but appears to have inconsistent effects on high-density lipoprotein (HDL-C) or triglycerides (TG); Resistance training seems to reduce LDL-C and TG levels by 6-9 mg dL-1, while HDL-C has no effect. Among them, the decrease in LDL-C also represents a reduction in the risk of hypertension [9].

Cornelissen and Smart (2013) conducted a systematic review to explore the effects of different exercise training on blood pressure changes, and pointed out that aerobic

endurance training, dynamic resistance training, and isometric training can all reduce systolic and diastolic blood pressure, while comprehensive training can only reduce diastolic blood pressure [10]. However, a few studies on isometric contraction training have shown that this form of training has the potential to minimize systolic blood pressure to the greatest extent possible [11] [12]. The reason why isometric contraction training is currently believed to lower blood pressure may be due to enhanced neural regulation, improved oxidative stress, and improved endothelial function.

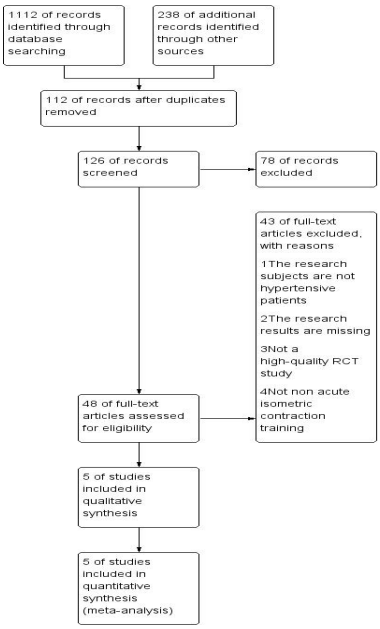

Figure 1. Systematic Overview Preferred Report Project Flow Chart

Based on the current lack of research comparing the effect of equal length contraction training on blood pressure improvement, this article searched Pubmed, Web of Science, and Google Scholar literature databases to compile literature on the use of equal length contraction training as a blood pressure lowering strategy from 2000 to 2024, exploring the correlation between experimental methods and the degree of blood pressure reduction, and attempting to find more effective non pharmacological treatment strategies for hypertension. Seven studies were included in the research data, with the inclusion criteria being empirical studies and the use of isometric contraction training as an intervention to lower blood pressure; The exclusion condition is the

simultaneous use of antihypertensive drugs or other factors that may affect blood pressure.

Long term intervention of isometric contraction

Table 1. The effect of long-term isometric contraction training on blood pressure

Study and country	Participants	Duration,wk	Frequency	Exercise Training Characteristics
Daniel,2023,Colombia	CG:M 22 EG Handgrip:M 28 EG wall squat:M 27	12	3d/wk	4×2-min isometric contraction with 2 min of rest between each rep
Breno，2018,Brazil	CG:M 7andF 17 EG home based IHT:M 7and F 17 EG super based IHT:M7 and F 17	12	3d/wk	4 × 2 min at 30% of maximal voluntary contraction, with 1-min rest between bouts, alternating the hands
Palmeira,2021,Brazil	CG:M 10 and F 22 EG 30%MVC:M 9 and F 22	12	3d/wk	4x2 minutes at 30% of maximal voluntary contraction, one-minute rest between bouts, alternating the hands
Gustavo，2018，Brazil	CG:M 4 EG S30%2min:M 4 EG S50%2min:M 4 EG S30%3min:M 4	6	3d/wk	4 x 2 min at 30% and 50% of the maximal voluntary contraction(S30%)
Nemoto,2021,Japan	CG:M 15 F 7 EG 30%MCV:M 15 F 6	8	3d/wk	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

CG, control group; EG, experimental group; F, female; Fx, training frequency; HR peak, heart rate peak; IHG, isometric handgrip; IRT, isometric resistance training; low INT, low intensity; M, male; mixed, both sexes; MVC, maximal voluntary contraction.

This article includes a total of 5 studies that used equal length contraction as a long-term intervention for more than 6 weeks. The studies were published between 2013 and 2022, with 9 intervention groups and 238 hypertensive patients (intervention group, n=112; control group, n=116). The 5 studies used parallel designs, while the remaining studies used crossover designs. Three studies used parallel designs, while the remaining studies used crossover designs. Out of the 5 studies, 3 included participants of both genders,

while 2 studies only included males and there are no reports indicating that only females were included. Generally speaking, research reports on how they measure BP; Four studies reported using an automatic brachial artery blood pressure monitor to measure blood pressure, and one study used an automatic blood pressure monitor to measure blood pressure (Table 1).

Most studies monitor the strength of isometric contractions using maximum voluntary contraction (MVC) as a reference. Taking Ogbutor et al.'s (2019) study as an example, a grip strength meter is used to measure upper limb MVC. During the measurement, participants are required to hold the grip strength meter as hard as possible for 2 seconds, rest for 5 minutes, and then measure again. The average of the two test results can be used to obtain the MVC [13]. There is no fixed measurement method for determining MVC, but most studies use similar measurement methods, and the maximum force maintained in seconds may be between 2 and 5 seconds. In the studies included in this article, a total of 3 studies used 30% MVC, 1 study measured the differences between 30% MVC 1min, 50% 1min, and 30% MVC 3min, and 1 study used grip strength and wall squatting as references.

This article attempts to explain the effect of isometric contraction training on blood pressure by analyzing the differences in experimental methods. In the study using 30% MVC as the contraction strength, after 6-12 weeks of training three days a week, the blood pressure of all experimental participants significantly decreased.

There are three studies that focus on the upper limbs and use 30% MVC intensity for isometric contraction training. After 8 weeks and 14 weeks of training, the blood pressure of the experimental participants significantly decreased. However, the experimental participants in these two studies had vastly different conditions. Nemoto's experimental participants were 56.6% male, with an average age of 61 years old, and had blood pressure levels of SBP: 135.3 ± 9.5 mmHg and DBP: 81.2 ± 9.3 mmHg [14], while Palmeria was a primary healthcare unit (30-79 years old) with hypertensive female patients with pre hypertension (SBP: 129 ± 4 mmHg; DBP: 83 ± 3). The results showed that Nemoto's experimental participants had a decrease in systolic blood pressure of 2mmHg [15], while Palmeria's was 7mmHg, suggesting that this may be due to better control of blood pressure levels in primary healthcare patients. Nemoto's experimental participants had a decrease in systolic blood pressure due to values measured after home training. Low compliance with exercise and small numerical differences. The same results were also presented in Breno et al.'s (2018) study, which compared 72 experimental participants who received upper limb isometric contraction training in two different exercise venues for 12 weeks, three times a week. In the study, the systolic and diastolic blood pressure of the family group decreased by 4.2mmHg; The monitoring group showed a decrease of 12.5mmHg. From this, it can be seen that groups with supervision usually have better results and significantly lower blood pressure [16]. However, so far there have been no long-term intervention studies attempting to use monitoring methods other than in the laboratory, so it is still uncertain whether there is a correlation between the degree of contraction during long-term intervention and the exercise site.

FIGURE 2. (A) Position for initial wall squat evaluation (B)Wall squat training (C) Handgrip training.

In Daniel et al.'s (2023) experiment, two questions were attempted to be addressed: firstly, whether isometric contraction training can lower blood pressure; The second is to compare the degree of blood pressure reduction between grip strength and wall squatting training. The experiment divided 77 untreated adults with hypertension (SBP ≥ 130 mmHg) into a grip strength group, a squatting wall group, and a control group, with an intensity set at 30% MVC. Data collection and analysis were conducted on both systolic and diastolic blood pressure. Measure clinic blood pressure (BP) at baseline, after Phase 1 study, and after Phase 2 study. After the first stage, the average decrease in SBP in the handshake group (-11.2 mmHg, n=28) and squat group (-12.9 mmHg, n=27) was significantly greater than that in the control group (-0.4 mmHg; n=22), but there was no change in DBP. There was no significant intra group change in stage 2, but the systolic blood pressure was 3.8 mmHg. Although both interventions resulted in significant reductions in SBP, squatting on the wall seems to be more effective in maintaining the benefits of minimal training doses, and it may become an effective intervention for treating hypertensive patients [17].

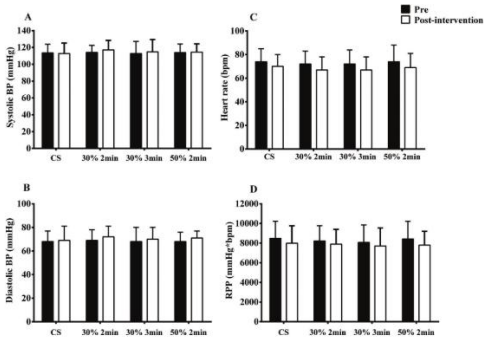

Figure 2. Systolic (A) and diastolic (B) blood pressure (BP), heart rate (C), and rate-pressure product (RPP- D) before and after a session of handgrip exercise with different intensities and volumes. CS - control session.

Compared to sports venues and training methods, Gustavo et al. (2018) randomly divided 12 hypertensive patients (58 ± 5 years old) into four equal length grip strength training stages: 4 × 2 min at 30% maximum voluntary contraction (S30%); At 50% maximum voluntary contraction, 4 × 2 min (S50% 2min); 4x 3 min, 30% maximum autonomous contraction (S30% 3 min); And the control period. Measure systolic and diastolic blood pressure, heart rate, and heart rate blood pressure product before and after exercise (at the 30th minute). Result: No significant changes were observed in cardiovascular variables after any treatment course (all comparisons were p40.05) [18]. Although this result indicates that equal strength grip exercises of different intensities and durations cannot lower blood pressure in hypertensive patients, there have been no long-term intervention studies attempting to set up experiments with multiple intensity and time variables. Therefore, it is still uncertain whether different intensities and

durations during long-term intervention are not associated with the degree of blood pressure decrease.
Based on the above, the reasons that may affect the experimental results may be related to whether the participants were supervised and the training methods used. When experimental participants suffer from hypertension, they usually experience significant improvements in systolic blood pressure, diastolic blood pressure, and mean arterial pressure after several weeks of training. However, there is no research on the duration of such effects after stopping training, and further exploration is needed in the future.

Acute intervention of isometric contraction

Table 2. Effects of Acute Isometric Contraction on Blood Pressure

Study and country	Participants	Duration,h	Detection Frequency	Exercise Training Characteristics
Bertplettii,2022,Brazil	CG 0.3%MVC:M 18 and F 14 EG 30%MVC:M 17 andF 15	24h	15 minutes before and after intervention	4×2-min isometric contraction with 2 min of rest between each rep
Olher Rdos，2013,Brazil	CG:F 4 EG 30%MVC:F 4 EG 50%MVC:F 4	72h	After intervention 5, 10, 15, 30, 45, and 60 minutes	4 × 2 min at 30% of maximal voluntary contraction, with 1-min rest between bouts, alternating the hands

Compared to long-term interventions, there are only 2 acute studies using isometric contractions as blood pressure control (Table 2). In an acute intervention study, 72 mixed male and female participants underwent a one-time equal length contraction exercise, with a maximum intensity of 30% MVC for 2 minutes of grip strength equal length contraction and 1 minute of rest time, for a total of 4 cycles. The results showed that although equal length contraction training did not cause any discomfort or adverse reactions, compared to pre intervention blood pressure data, systolic and diastolic blood pressure increased by 13 and 14 mmHg, respectively ($p<.05$). One minute after exercise, heart rate, systolic blood pressure, and diastolic blood pressure almost return to baseline [19]. Although hemodynamic responses were observed through isometric contractions in this study, the difference between resting state and end of exercise was minimal. From a physiological perspective, the intensity of isometric contractions is 30% of the maximum autonomous contraction force, which does not cause significant activation of the vagus nerve, resulting in almost no change in heart rate. It is speculated that the changes in systolic and diastolic blood pressure values mainly reflect a small increase in peripheral vascular resistance caused by arterial occlusion in the muscle contraction area, while there is no significant change in cardiac output.
In the study by Olher Rdos et al. (2013), they used different intervention regimens and tested two intensity conditions, 30% MVC and 50% MVC, including four groups with

five 10 second contractions per group. And besides before exercise, diastolic and systolic blood pressure were also measured during exercise and at 5, 10, 15, 30, 45, and 60 minutes after exercise. Although such intervention conditions did not cause adverse reactions in elderly women with hypertension in the experiment, they did not have a positive effect on lowering blood pressure. During exercise, there was a slight increase in blood pressure, but after exercise, blood pressure returned to baseline, which is consistent with the results of Bertpletti et al. [20].
Therefore, it can be concluded from the above two studies that acute intervention of isometric contraction training does not have adverse effects on the study subjects, but it also does not lower blood pressure. Due to the limited number of research articles and the fact that only one study focused on individuals with pre hypertension (SBP: 121 ± 10 mmHg; DBP: 74 ± 9 mmHg), further literature support is needed in the future. Currently, it is not sufficient to conclude that acute intervention of isometric contraction training has no positive effect on blood pressure reduction.

Conclusions

IHG can significantly reduce SBP、DBP and MAP in hypertensive patients. Therefore, we recommend that this type of exercise (especially wall squatting and grip strength exercises) is considered an effective therapy for reducing arterial hypertension. The efficiency of this intervention is limited to the short term. Therefore, long-term effects (at least 1 year) should be studied.

Disclosure

Author's contribution

Authors have read and agreed with the published version of the manuscript.

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Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Conflict of interest

The authors deny any conflict of interest.

References:

[1]Health Promotion Administration, Ministry of Health and Welfare (Jul 12, 2019). San gao fang zhi zhuan qu ”gao xie ya, gao xie zhi, tang niao bing”. https://www.hpa.gov.tw/Pages/List.aspx?nodeid=1463

[2]National Cardiovascular Center.2023.Chinese Cardiovascular Health and Disease Report(Access: 29.04.2010).https://www.nccd.org.cn

[3]Centers for disease control and prevention. (September 27, 2021). Facts About Hypertension. https://www.cdc.gov/ bloodpressure/facts.htm

[4]American College of Cardiology. (Jun 21, 2021).New guidance on blood pressure management in low-risk adults with stage 1 hypertension.https://www.acc.org/latest-in

-cardiology/articles/2021/06/21/13/05/new-guidance-on-bp- management-in-low-risk-adults-with-stage-1-htn

[5]Cornelissen, V. A., & Smart,N. A. (2013). Exercise training for blood pressure: A systematic review and meta-analysis. Journal of the American Heart Association, 2(1), 004473. https://doi. org/10.1161/jaha.112.004473

[6]Juraschek, S. P., Woodward, M., Sacks, F. M., Carey, V. J., Miller, E. R., 3rd, & Appel, L. J. (2017). Time course of change in blood pressurefrom sodium reduction and the DASH diet.Hypertension, 70(5), 923-929. https://doi.org/ 10.1161/hypertensionaha.117.10017

[7]Fagard, R. H. (2001). Exercise characteristics and the blood pressure response to dynamic physical training. Medicine & Science in Sports &Exercise, 33(6), 484-492. https://doi.org/ 10.1097/00005768-200106001-00018

[8]Mughal, M. A., Alvi, I. A., Akhund, I. A., & Ansari, A. K. (2001). The effects of aerobic exercise training on resting blood pressure in hypertensive patients. Journal of the Pakistan Medical Association, 51(6), 222-226.https://www.jpma.org.pk/article-details/2674?article_id=2674CachedYou

[9]Eckel, R. H., Jakicic, J. M., Ard, J. D., de Jesus, J. M., Houston Miller, N., Hubbard, V. S., Lee, I.M., Lichtenstein,A. H., Loria, C. M., Millen, B. E., Nonas, C. A., Sacks, F. M., SmithJr, S. C.,Svetkey, L. P., Wadden, T. A., & Yanovski, S. Z. (2014). 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation,129(25 Suppl 2), 76-99. https://doi.org/ 10.1161/01.cir.0000437740.48606.d1

[10]Cornelissen, V. A., & Smart,N. A. (2013). Exercise training for blood pressure: A systematic review and meta-analysis. Journal of the American Heart Association, 2(1), 004473. https://doi. org/10.1161/jaha.112.004473

[11]Carlson, D. J., Dieberg, G., Hess, N. C., Millar, P. J., & Smart, N. A. (2014). Isometric exercise training for blood pressure management: A systematic review and meta-analysis. Mayo Clinic Proceedings, 89(3), 327-334.https://doi.org/10.1016/j.mayocp.2013.10.030

[12]Inder, J. D., Carlson, D. J., Dieberg, G., McFarlane, J. R., Hess,N. C., & Smart,N. A. (2016).Isometric exercise training for blood pressure management: A systematic review and meta-analysis to optimize benefit. Hypertension Research, 39(2), 88-94. https://doi.org/ 10.1038/hr.2015.111

[13]Ogbutor, G. U., Nwangwa, E. K., & Uyagu, D. D. (2019). Isometric handgrip exercise training attenuates blood pressure in prehypertensive subjects at 30% maximum voluntarycontraction. Nigerian Journal of Clinical Practice, 22(12), 1765-1771.https://doi.org/10.4103/njcp.njcp_240_18

[14]Nemoto,Yuki,et al."Effects of Isometric Handgrip Training on Home Blood Pressure Measurements in Hypertensive Patients: A Randomized Crossover Study".Internal Medicine,vol.60,2021,pp.2181-2188,https://doi.org/10.2169/internalmedicine.5865-20.

[15]Palmeira,Aline Cabral,et al."Effects of isometric handgrip training on blood pressure among hypertensive patients seen within public primary healthcare: a randomized controlled trial".Sao Paulo Medical Journal,vol.139,2021,pp.648-656,https://doi.org/10.1590/1516-3180.2020.0796.R1.22042021.

[16]Farah,Breno Q.,et al."Supervised, but Not Home-Based, Isometric Training Improves Brachial and Central Blood Pressure in Medicated Hypertensive Patients: A Randomized Controlled Trial".Frontiers in Physiology,vol.9,2018,https://doi.org/10.3389/fphys.2018.00961.

[17]Cohen,Daniel D,et al."Reductions in systolic blood pressure achieved by hypertensives with three isometric training sessions per week are maintained with a single session per week".The Journal of Clinical Hypertension,vol.25,2023,pp.380-387,https://doi.org/10.1111/jch.14621.

[18]Silva,Gustavo O,et al."Acute blood pressure responses after different isometric handgrip protocols in hypertensive patients".Clinics,vol.73,2018,pp.e373,https://doi.org/10.6061/clinics/2018/e373.

[19]Bertoletti,Otávio A.,et al."Isometric handgrip exercise impacts only on very short-term blood pressure variability, but not on short-term blood pressure variability in hypertensive individuals: A randomized controlled trial".Frontiers in Physiology,vol.13,2022,https://doi.org/10.3389/fphys.2022.962125.

[20]Olher Rdos, R., Bocalini, D. S., Bacurau, R. F.,Rodriguez, D., Figueira, A., Jr., Pontes, F. L., Jr, Navarro, F. N., Simoes, H. G., Araujo, R. C.,& Moraes, M. R. (2013). Isometric handgrip does not elicit cardiovascular overload or post-exercise hypotension in hypertensive older women. Clinical Interventions in Aging, 8, 649- 655. https://doi.org/10.2147/cia.s40560