Scientific Evidence that Isometric Exercise Reduces Blood Pressure

Purpose

This paper has been prepared for the purpose of:

1) defining the problem of high blood pressure
2) reviewing indirect evidence of isometrics lowering of blood pressure
3) showing the direct evidence that controlled isometric exercise can reduce and maintain blood pressures in humans
4) providing evidence from recent studies of physiological mechanisms modified by the isometric training which contribute to the blood pressure reduction and control.
5) summarizing mechanisms theory, supported by published medical research, which explains the relationship of isometric training to blood pressure reduction and control

Background

Hypertension is defined as a diastolic blood pressure of 90 mmHg or higher and/or a systolic pressure of 140 mmHg or higher. It is present in an estimated 50 -60 million Americans and is more common in blacks and older adults[1]. Hypertension is a leading risk factor for coronary heart disease, congestive heart failure, stroke, ruptured aortic aneurysm, renal disease, and retinopathy. These complications of hypertension are among the most common and serious diseases in the U.S., and successful efforts to lower blood pressure could thus have substantial impact on population morbidity and mortality. Heart disease is the leading cause of death in the U.S., accounting for nearly 740,000 deaths each year (287 deaths per 100,000 population), and cerebrovascular disease, the third leading cause of death, accounts for about 150,000 deaths each year (58/100,000). Milder forms of hypertension predict progression to more severe elevations and development of cardiovascular disease. Coronary heart disease mortality begins to increase at systolic blood pressures above 110 mmHg and at diastolic pressures above 70 mmHg.

Results from the Framingham Heart Study show that the benefit of reducing blood pressure, by even a few mmHg, leads to significant reductions in the risk of coronary heart disease and stroke incidents.[2] A reduction of diastolic blood pressure of only 2 mmHg leads to a 9% reduction of coronary heart disease, and a 15% reduction in stroke incidents. A 7.5 mmHg reduction leads to a 29% reduction of coronary heart disease, and a 48% reduction in stroke incidents. This new isometric exercise therapy is a very important finding, considering the large blood pressure reductions that are obtained, and the correspondingly large reduction of cardiovascular risk factors it provides.

Indirect evidence of the effect of isometrics on resting blood pressure.

The 1985 report by Buck and Donner[3] studied the relationship between occupational isometric activity and incidence of hypertension. Their study found that males with moderate to high isometric content in their job function had a 7.4% incidence of five-year hypertension, compared to 10.4% of those in jobs with low isometric activity. This is a 29% reduction in the incidence rate attributed to the daily isometric content of the job function. This study included over 4,000 men, from low, middle, and upper social classes. Their result is the largest study to date of the relationship between isometric exercise and hypertension.

Isometric contractions, if held for extended periods, lead to increases in both systolic and diastolic blood pressure. This fact was being used to investigate the ability of U.S. Airforce pilots to withstand high "g" load maneuvers in the cockpits of airplanes. It was found that isometrics could extend the "g" range of a pilot, thus enhancing their ability to out maneuver their enemies. This research involved controlled isometric handgrip contractions. The protocol was to measure a resting blood pressure, measure blood pressure while performing the contractions, and measure blood pressure after the contractions until a return to pre-exercise level was attained. It was noticed, as this project continued over several weeks, that the test subject's initial resting blood pressures were decreasing. This was the first observation of controlled isometric handgrip efforts having an effect of lowering resting blood pressure.

Controlled studies were needed to determine the exact combination of isometric force, duration of exertions, rest periods in an interrupted exercise, and number of repetitions for an effective protocol. The CardioGrip® protocol was developed as a means to consistently instruct users in performing the isometric exercise protocol so they could optimize

MD Systems, Inc. P.O. Box 1647
Westerville, Ohio 43086
ph (614) 818-3000 fax (614) 818-3182
www.mdsystems.com

the blood pressure reduction benefits of isometric therapy while minimizing physical stress and duration of effort. The protocol consists of brief, interrupted, sub-maximal, isometric hand contractions. Each hand contraction lasts two minutes or less (depending upon protocol selected), is separated from the next effort by a one minute rest period, and is repeated with alternate hands for a total of four efforts. The entire exercise takes less than 12 minutes to perform. This protocol is then performed regularly, from 3 to 7 times per week.

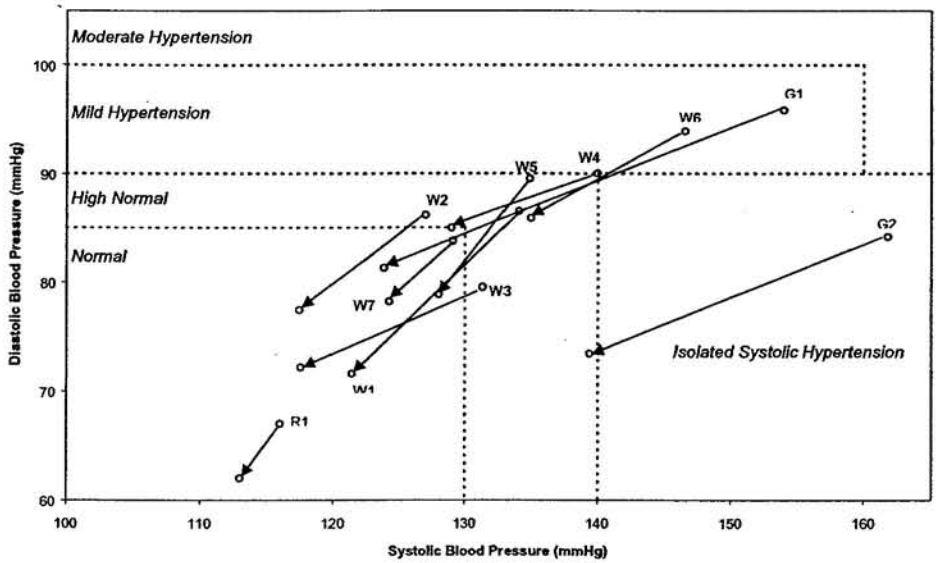
Direct evidence of the CardioGrip® protocol lowering resting blood pressure.

Clinical trials[4-8] have shown that the CardioGrip® protocol has led to blood pressure reductions in those subjects tested. This effect is achieved in 4 to 8 weeks, and can be maintained for a period greater than one year. Table 1 summarizes these results.

Study	# in study	# weeks	Average Pre SBP	Average Pre DBP	Drop in SBP	Drop in DBP
W1	8	8	134.1	86.5	12.7	14.9
W1 control	7	8	134.0	83.4	-2.2	-1.6
W2	10	5	127.0	86.2	9.5	8.8
W3	20	12	131.4	79.5	13.8	7.3
W3 control	20	12	125.0	76.0	-1.0	-1.0
W4	9	5	140.0	90.0	11.0	5.0
W5	7	8	134.9	89.5	6.9	10.7
W6	13	4	146.6	93.9	11.6	8.0
W7	8	6	129.1	83.8	4.9	5.6
G1	4	>52	154.0	95.8	30.2	14.5
G2	8	13-81	161.8	84.2	22.4	10.8
R1	9	5	116.0	67.0	3.0	5.0

Table 1. Results of clinical trials using the CardioGrip® protocol.

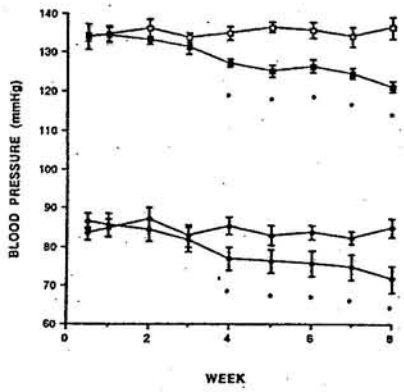
These trials covered a broad range of individuals, from normal blood pressure, well into the hypertensive range. Plotting the entry and exit blood pressures, it is readily seen that all groups had a significant lowering of blood pressure during the weeks of performing the CardioGrip® protocol. All groups follow the same trend, lowering of both systolic and diastolic blood pressure. Each of these trials included at least 4 weeks of exercise training using the CardioGrip®



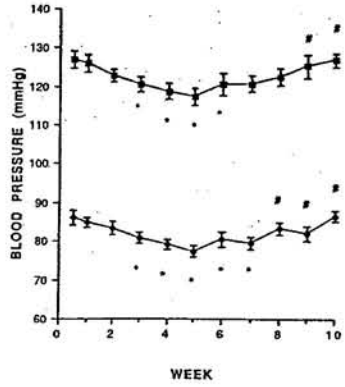
MD Systems, Inc. P.O. Box 1647
Westerville, Ohio 43086
ph (614) 818-3000 fax (614) 818-3182
www.mdsystems.com

protocol. Most individuals performed the exercise for no more than 12 weeks. The exact format of each study has been summarized to allow comparisons across studies included in this summary.

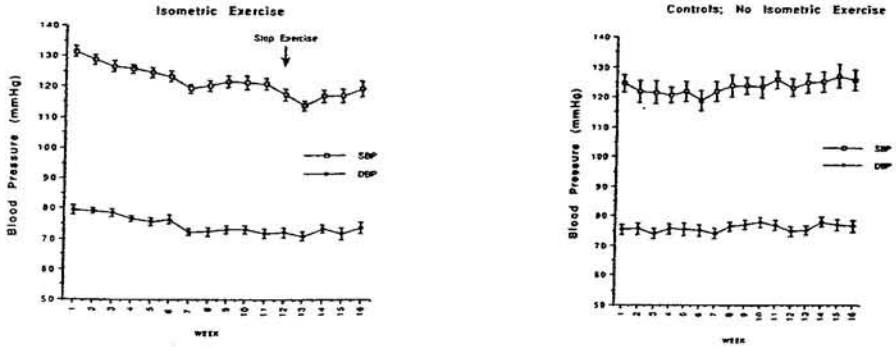
Study W1[4]: This study was a randomized controlled study involving 15 healthy volunteers (8 in the exercise group and 7 in the control group) with resting blood pressure levels in the upper end of the normal range. Subjects were sought in this range as a cautious approach in the first-ever controlled study before moving on to subjects with higher pressures. The exercise group conducted a systematic isometric exercise using the CardioGrip® protocol 3 days a week over an 8 week period. Both groups were instructed to maintain their normal lifestyle. None of the subjects were receiving any other treatment for their blood pressure. The results showed a mean reduction of systolic blood pressure (SBP) of 12.7 mmHg (134.1± 0.95 mmHg to 121.4 ± 1.34mmHg) and a mean reduction in diastolic blood pressure (DBP) of 14.9 mmHg (86.5± 2.01mmHg to 71.6 ± 3.50mmHg) in the exercise group and no change in resting blood pressure in the control group (initial: SBP; 134.0± 3.30 mmHg, DBP; 83.4 ± 1.67 mmHg, final: SBP; 136.6 ± 2.78 mmHg , DBP; 85.0 ± 2.43 mmHg) A reduction in blood pressure levels was seen in all subjects in the exercise group.



Study W2[4]: This study was a within patient comparison of the effects of the isometric exercise using the CardioGrip® protocol and no exercise. The exercise sessions were conducted 5 days/ week for 5 weeks until 24 sessions were completed (to compare with the 24 treatments in Study W1). During weeks 6 - 10, no isometric exercise was performed. Ten patients were enrolled in this study. The results showed a decline in both systolic blood pressure (SBP) and diastolic blood pressure (DBP) over the 5 week training period (initial: SBP; 127.0 ± 2.28, DBP; 86.2 ± 1.85, 5 weeks: SBP; 117.5 ± 2.23, DBP; 77.4 ± 1.49). Both the SBP and DBP returned to initial levels during the 6 - 10 week no exercise period, indicating that cessation of the isometric exercise protocol will result in a slow return in resting blood pressure.



Study W3[5]: This study was a randomized, control group study to evaluate the effects of the CardioGrip® isometric exercise program in patients participating in a Phase III of a cardiac rehabilitation program. This patient population consisted of patients that had suffered a heart attack, stroke or by-pass surgery and had worked up to a Phase III in a cardiac rehabilitation program (dynamic exercise). The exercise sessions were conducted 2 days/ week for 12 weeks. During weeks 13 - 16, no isometric exercise was performed. Forty-three patients were enrolled in the study (20 patients in the isometric exercise group and 23 matched controls). All patients continued their prescribed cardiac rehabilitation program while in this study. The results demonstrated that resting systolic blood pressure decreased significantly from an average of 131.4 to 117.6 mmHg over the 12 weeks of exercise. Resting diastolic blood pressure decreased significantly from 79.5 to 72.2. This is important because, although the patients were



within the normal range, at least the systolic blood pressure was above the "ideal" target of 120 mmHg. It also lends support to the desire to determine whether, after lowering blood pressure with isometric exercise, medications could be reduced or withdrawn. No change occurred in resting blood pressures in the control patients.

MD Systems, Inc. P.O. Box 1647
Westerville, Ohio 43086
ph (614) 818-3000 fax (614) 818-3182
www.mdsystems.com

Study W4[8]: This unpublished study was a cross-over comparison to evaluate the effect of conducting the CardioGrip® isometric exercise program one session per day versus two sessions per day. One of two schedules were performed (once a day or twice a day), 3 days/week over a 5 week period . Subjects then performed no sessions over a 3 months period and then performed the second schedule, 3 days/week for another 5 week period. Nine healthy volunteers were enrolled in the study with blood pressure levels in the upper end of the normal range. The result was that the group average blood pressures entering the study were 140/90 and declined to 129/85 mmHg. When repeated months later, similar starting pressures and similar declines were observed. This indicates that 2 per day exercises were not more beneficial than 1 per day.

Study W5[8]: This was an uncontrolled study to evaluate the effect of the CardioGrip® isometric exercise program in patients with borderline hypertension. Seven healthy volunteers with borderline hypertension were enrolled in the study. The result was that the group mean decline in blood pressure was from 134.9/89.5 to 128/78.8, for a decline of 6.9/10.7 mmHg. The decline fit a linear model, suggesting that continuation of the exercise for more than 8 weeks might have led to a further decrease in blood pressure.

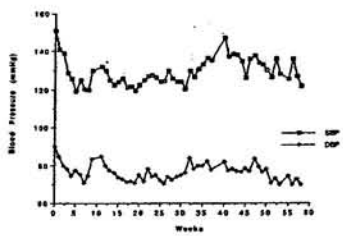
Study W6 (a&b)[8]: This study was a parallel group comparison of two isometric exercise programs, one program involved the performance of 1 isometric contraction per session per day, and the second program involved performing 6 isometric contractions per session. Seven subjects participated in the first program and 6 subjects participated in the second program. All subjects had blood pressure levels in the upper end of the normal range or in the hypertensive range. The result for the first group was that the average systolic blood pressure decreased from 144.6 to 132.6 mmHg, and diastolic from 92.6 to 82.9 mmHg; decreases of 12.0/9.7 mmHg. The result for the second group was that the average systolic blood pressure declined from 149.0 to 137.8, and the diastolic declined from 95.5 to 89.5 mmHg., decreases of 11.2/6.0 mmHg.

Study W7[8]: This study was conducted to evaluate the effect of the CardioGrip® isometric exercise program to simultaneously reduce both blood pressure and blood cholesterol and total lipids. The protocol prescribed conducting the isometric exercise 4 days/week for 6 weeks. The result was that resting blood pressure averages for the group changed from 129.1/83.8 to 124.2/78.2, for a decline of 4.9/5.6 mmHg. While the group mean data for cholesterol and total lipids did not show a significant change, it appeared that some individuals showed a trend for a desirable shift in lipids. The lipid results are likely due to recruiting subjects whose lipid levels were not dramatically different from normal at the start.

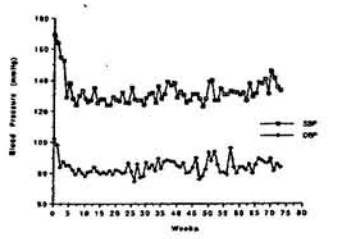
Study G1[6]: This study was a case study to evaluate the effects of the CardioGrip® isometric exercise over a 1 year period in patients with high normal to high blood pressure. The protocol design was for the patients to perform the isometric exercise 3 times/week, with the criterion that they must average at least 2 exercise sessions per week and not miss more than 6 consecutive sessions. Each patient experienced large decreases in resting blood pressure within a few weeks of the study, with some showing declines over several more weeks. A description of each patient's experience is given below:

There were four individuals who completed the study:

1) A 73 year old woman entered the study with blood pressures 151/90 mmHg. Her pressure dropped dramatically over several weeks, during which time the physician first cut her dosage, then withdrew her 2 drugs for hypertension entirely. She experienced a decline in blood pressure to 122/70 mmHg in the final week, for a decrease of 29/20 mmHg over her 58 weeks of participation.



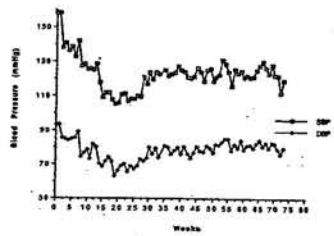
2) A 48 year old male started at 168/102 mmHg, experienced a drop in blood pressure over several weeks into the normal range and maintained normal pressures through his 73 weeks, at which time his pressure in the last week was 132/84 mmHg, for a total decline of 36/18 mmHg. He was taking several drugs for other reasons, but no hypertensive medications during the study.



MD Systems, Inc. P.O. Box 1647
Westerville, Ohio 43086
ph (614) 818-3000 fax (614) 818-3182
www.mdsystems.com

3) A 43 year old male, on anti-hypertensive medication, started at 139/98. At week 19 his physician changed him to another anti-hypertensive medication, then withdrew that one at week 26. At week 53 his pressure of 121/87 represented a decline of 19/12 mmHg.

4) A 69 year old male entered the study with a blood pressure of 158/93 mmHg, on medications for other reasons, but no anti-hypertensive drugs. Over about 20 weeks his pressure dropped to quite low in the normal range, rebounded somewhat to settle out in the middle of the normal range, and was 119/80 mmHg at week 73, a decline of 39/13 mmHg.



Study G2[6]: This study was a case study to evaluate the effects of the CardioGrip® isometric exercise over a 1 year period in patients with high normal to high blood pressure. The protocol design was the same as for G1, above. These patients are the ones who did not meet the criteria of average sessions per week, or who did not stay in the study for the full year. Each patient experienced large decreases in resting blood pressure within a few weeks of the study, with some showing declines over several more weeks. A description of each patient's experience is given below.

There were eight individuals who participated in the study:

1) A 47 year old male entered with blood pressure of 154/98 on 2 anti-hypertensive drugs, which were withdrawn at the end of week 5 with a blood pressure at that time of 122/81, continued through week 58. Although he averaged only 0.9 visits per week, his blood pressure at week 58 was 128/88, for a decline of 26/10 mmHg.

2) A 64 year old female started with a blood pressure of 155/98 mmHg and declined to 134/80 in 13 weeks, for a decline of 21/18, before dropping out of the study.

3) A 64 year old female entered with a blood pressure of 168/85 mmHg and declined by 28/10 to 140/75 mmHg in 81 weeks.

4) A 64 year old male entered with a blood pressure of 153/89 and declined by 10/9 to 143/80 in 76 weeks.

5) A 61 year old female entered at 157/64 and declined by 29/6 to 128/58 mmHg by week 69.

6) An 82 year old female entered at 152/73 and declined by 15/2 to 137/71 in week 43.

7) An 87 year old female entered at 177/81 and declined by 28/7 to 149/74 in week 28.

8) Individual entered at 178/86 and declined by 30/18 to 148/68 in week 30.

Study R1[7]: This study was a randomized control group study to evaluate any change in control of the blood vessels by the sympathetic nervous system after isometric exercise using the CardioGrip® protocol. Seventeen healthy volunteers were enrolled in the study (9 in the exercise group and 8 in the control group). The exercise group conducted the systematic isometric exercise using the CardioGrip® protocol 3 days a week over an 8 week period. Both groups were instructed to maintain their normal lifestyle. None of the subjects were receiving any other treatment for their blood pressure. The result was that diastolic blood pressures were significantly decreased (67 to 62 mmHg on average) even though the initial blood pressure average for the group was quite normal. Systolic blood pressure showed a trend to be lower, but was not significant statistically (116 to 113 mmHg). The nerve recordings did not show a change comparing them before and after training.

MD Systems, Inc. P.O. Box 1647
Westerville, Ohio 43086
ph (614) 818-3000 fax (614) 818-3182
www.mdsystems.com

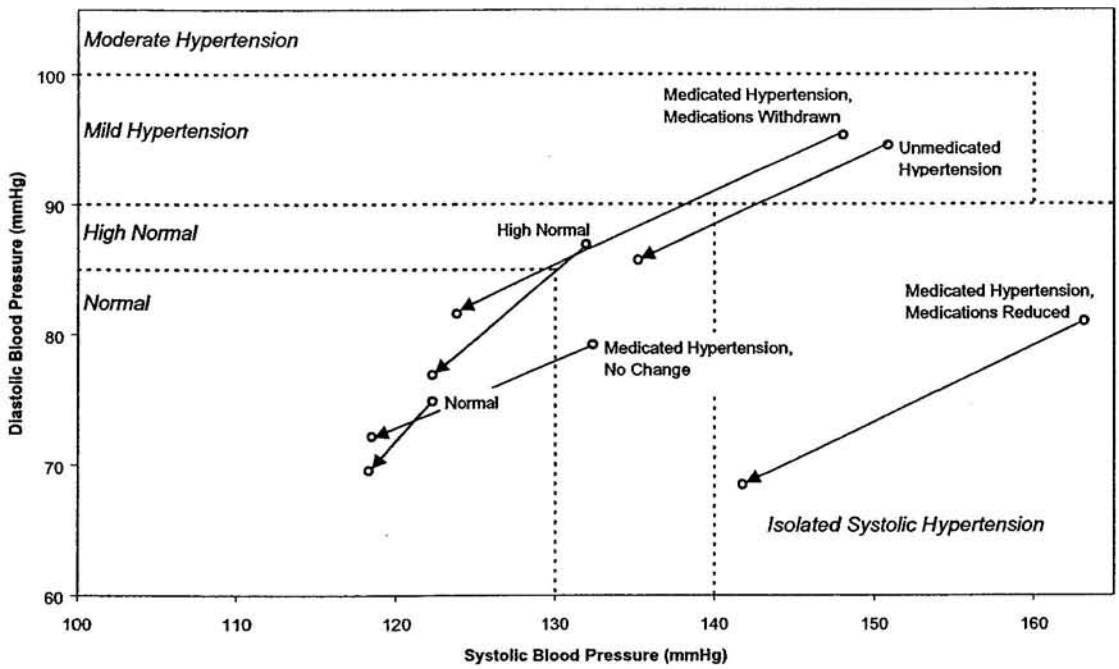
Treatment areas to be addressed:

Reviewing the clinical trials, it becomes evident that the effect of isometric exercise on lowering blood pressure is not limited to any particular range of pre-exercise blood pressure. A wide range of entry blood pressures are included in these studies, many have been stable on anti-hypertensive medication, many have been on anti-hypertensive medication and either reduced or withdrawn from those medications. These results show that this isometric training is an effective tool in the treatment of high blood pressure

Starting Blood Pressure Range	Data Source: Number	Total in Range	Average Starting SBP	Average Starting DBP	Average Drop in SBP	Average Drop in DBP	Action during the trial
Normal	R1:9, W7:8	17	122.2	74.9	3.9	5.3	None
Normal *Controls*	W1C:7	7	134.0	83.4	-2.2	-1.6	None
High Normal	W1:8, W2:10, W4:5, W5:7, W6a:1	31	132.0	86.9	9.8	10.0	None
Unmedicated Hypertension	G1:2, G2:2, W4:4, W6a:6, W6b:6	20	150.9	94.5	15.7	8.8	None
Medicated Hypertension	G2:1, W3:20	21	132.4	79.2	13.9	7.0	None
Medicated Hypertension *Controls*	W3C:20	20	125.0	76.0	-1.0	-1.0	None
Medicated Hypertension	G2:4	4	163.2	81.0	21.4	12.5	Medications Reduced
Medicated Hypertension	G1:2, G2:1	3	148.0	95.3	24.3	13.7	Medications Withdrawn

Table 2. Data summarized as to entry blood pressure and medication profiles

Plotting the entry and exit blood pressures, for this grouping of the individuals, it is readily seen that all groups had a significant lowering of blood pressure during the weeks of performing the CardioGrip® protocol. All groups follow the same trend, lowering of both systolic and diastolic blood pressure.



MD Systems, Inc. P.O. Box 1647
Westerville, Ohio 43086
ph (614) 818-3000 fax (614) 818-3182
www.mdsystems.com

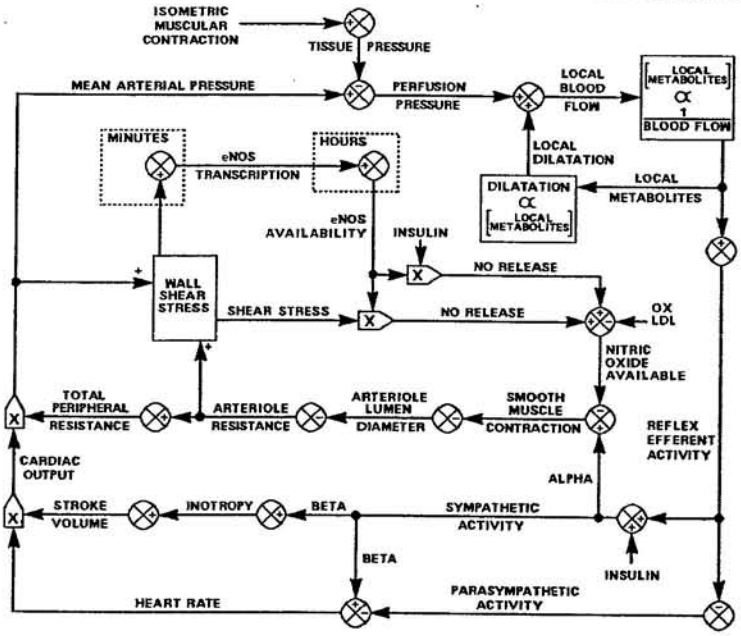
Recent studies verifying effectiveness and evidence for mechanisms

Study M1 (in review for publication): This study[8] examined the effects of isometric handgrip training on resting arterial blood pressure, heart rate variability and blood pressure variability. Nine subjects in a senior citizen exercise (rhythmic) program had the CardioGrip protocol added to their routine and 8 control subjects made no change in their exercise program. The protocol was that of study W1, above. A significant group mean systolic blood pressure decrease of 9,4 mmHg (+/-7.8) occurred. Diastolic group mean pressures did not change significantly but declined from 82 (+/-9.3) to 75 (+/-10.9) mmHg. That the change was not significant is not surprising given that their initial diastolic pressures were normal, whereas their initial systolic pressures averaged 157 mmHg. The analysis of blood pressure variability from beat to beat, by Fourier analyses, indicated a decrease in sympathetic activity and an increase in parasympathetic activity, and was interpreted as contributing to a decrease in peripheral resistance, thus participating in the decline in systolic blood pressure.

Study H1: In a study [9] whose primary purpose was to evaluate changes in orthostatic tolerance (increased heart rate or symptoms of fainting) with isometric exercise training, both arm and leg isometric training was employed. Resting systolic blood pressure significantly decreased with both leg (decreases averaged 10+/-8.7 mm Hg) and arm (decreases of 12.4+/- 9.3 mmHg) training for 5 weeks.

Theoretical mechanism of peripheral resistance regulation by nitric oxide.

It is known that nitric oxide (NO) release is increased in response to increased shear stress in blood vessels, especially in the smaller arterioles [9]. This stress on endothelial cells lining the vessels activates the enzyme, nitric oxide synthase (eNOS) to result in releasing nitric oxide from the substrate L-arginine. NO interacts with smooth muscles outside the endothelium, resulting in relaxation, contributing to vasodilation, lowering vascular tone. Further, it has been shown that repeated shear stress regulates the genetic transcription controlling the eNOS enzyme production capability [11]. Isometric muscular contractions provide a method of imposing such shear stress systemically within the cardiovascular system. Under shear stress, endothelial cells also undergo alignment with the direction of blood flow [12], producing structural changes which are consistent with a reduction of resistance to flow that contributes to lower blood pressure.



Since the discovery of the vasodilating effects of nitric oxide, numerous studies of its origin, effects and genetic control have been completed. These studies enable a theoretical proposal of mechanisms impacted by isometric therapy (see illustration). Study M1, described above, demonstrated a decrease in sympathetic activity and an increase in parasympathetic activity following imposition of shear stress of isometric exercise. This result confirms an important element in the mechanisms theory ascribed to isometric training and its lowering of blood pressure. However, it is noted that no studies are known to have been completed yet which directly measure responses of the release of nitric oxide resulting in vasodilation and lowering of blood pressure as a result of isometric exercise training. Yet the evidence is compelling and encourages studies of this nature to be done.

MD Systems, Inc. P.O. Box 1647
Westerville, Ohio 43086
ph (614) 818-3000 fax (614) 818-3182
www.mdsystems.com

Conclusion

This evidence clearly shows that the CardioGrip® protocol is useful in the treatment of high blood pressure as a *preventative* treatment, as a *primary* treatment, as a *supplement* in pharmacological treatment, as a *substitute* in pharmacological treatment and as a *replacement* to pharmacological treatment.

1) preventative: individuals with normal blood pressure have reduced their blood pressure & individuals with high normal blood pressure have reduced their blood pressure

2) primary: individuals with hypertension have reduced their blood pressure

3) supplement: individuals with hypertension, taking anti-hypertensive medications, have reduced their blood pressure

4) substitute: individuals with hypertension, taking anti-hypertensive medications, have reduced their blood pressure and had their anti-hypertensive medication reduced

5) replacement: individuals with hypertension, taking anti-hypertensive medications, have reduced their blood pressure and had their anti-hypertensive medication withdrawn

References

1. Chapter 3: Screening for hypertension, Guide to Clinical Preventive Services, Sec. Ed., 1996.
2. Cook, N. R., J. Cohen, P. R. Hebert, J. O. Taylor, C.H. Hennekens, Implications of small reductions in diastolic blood pressure for primary prevention, *Arch Intern Med* 155:701-709. 1995.
3. Buck, C. and A. P. Donner. Isometric occupational exercise and the incidence of hypertension. *J. Occup. Med. 27:370-372, 1985.*
4. Wiley, R. L., C. L. Dunn, R. H. Cox, N. A. Hueppchen, and M. S. Scott. Isometric exercise training lowers resting blood pressure. *Med Sci Sports Exerc* 24(7):749-754, 1992.
5. Summary of unpublished data: Wiley, R. L., H. I. Geisberg, "Blood pressure reduction in hypertensive cardiac rehabilitation patients".
6. Unpublished report: Geisberg, H. I., R. L. Wiley, "Blood pressure control with isometric exercise by hypertensive patients", 1996.
7. Ray, C. A., D. I. Carrasco, A. N. Martin, Effects of isometric handgrip training on blood pressure and muscle sympathetic nerve activity *The Physiologist* 39(5):A-17, 1996.
8. Taylor Ac, McCartney N, Kamath MV. Isometric training lowers resting blood pressure and modulates autonomic control. Submitted to *Med. Sci. Sports Exerc*
9. Howden R. Lightfoot JT, Brown SJ, Swaine IL. The effects of isometric exercise training on resting blood pressure and orthostatic tolerance in humans. *Exper. Physiol.* 2002:507-515
10. Koller A, Kaley G. Endothelial regulation of wall shear stress and blood flow on skeletal muscle microcirculation. *Am. J. Physiol.* 1991;260:H862-H868.
11. Ziegler T, Silacci P, Harrison VJ, Hayoz D. Nitric oxide synthase expression in endothelial cells exposed to mechanical forces. *Hypertension* 1998:32:351-355.
12. Davies PF. Flow-mediated endothelial mechanotransduction. *Physiol. Rev.* 1995;75:519-560.

MD Systems, Inc. P.O. Box 1647
Westerville, Ohio 43086
ph (614) 818-3000 fax (614) 818-3182
www.mdsystems.com