

Exercise in Hypertension

A Clinical Review

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Abstract

The current exercise prescription for the treatment of hypertension is: cardiovascular mode, for 20–60 minutes, 3–5 days per week, at 40–70% of maximum oxygen uptake ($\dot{V}O_{2max}$). Cardiovascular exercise training is the most effective mode of exercise in the prevention and treatment of hypertension. Resistance exercise is not the preferred mode of exercise treatment, but can be incorporated into an exercise regime provided the diastolic blood pressure response is within safe limits. It is inconclusive whether durations longer than 30 minutes produce significantly greater reductions in blood pressure. A frequency of three exercise sessions per week has been considered to be the minimal frequency for blood pressure reduction. **(Author: please confirm that rewording is ok)** Higher frequencies tended to produce greater reductions, although not significantly different. Evidence still exists that high intensity exercise ($>75\% \dot{V}O_{2max}$) may not be as effective as low intensity exercise ($<70\% \dot{V}O_{2max}$) in reducing elevated blood pressures. Exercise can be effective without a change in bodyweight or body fat. Bodyweight or body fat loss and anti-hypertensive medications do not have an added effect on blood pressure reduction associated with exercise. β -blockade is not the recommended anti-hypertensive medication for effective exercise performance in non-cardiac patients. Not all hypertensive patients respond to exercise treatment. Differences in genetics and pathophysiology may be responsible for the inability of some hypertensive patients to respond to

exercise. Ambulatory technology may allow advances in individualising a more effective exercise prescription for low- and non-responders.

As early as 1983, the World Health Organization recommended the use of non-pharmacological approaches in the primary and adjunctive treatment for hypertension.^[1] Nicholls considers exercise to be the most promising non-pharmacological treatment of hypertension.^[2] Organisations, including the American Heart Association,^[3,4] the American College of Sports Medicine,^[5] the Surgeon General of the United States,^[6] The National Institutes of Health,^[7] and the Centers for Disease Control^[8] have issued policy statements supporting the role of exercise treatment in hypertension.

Since 1982, the evidence supporting the role of exercise treatment of hypertension has been the subject of numerous reviews.^[9-21] The focus of these past reviews has been a scientific approach for researchers in exercise and hypertension. This review is unique in that exercise in the treatment of hypertension will be considered from a clinical perspective. General topics to be addressed include: (i) a summary of the current research findings; (ii) the current exercise prescription; (iii) the interaction of bodyweight, hypertension, and blood pressure reduction; (iv) the identification of who benefits from exercise treatment; (v) interaction of exercise and anti-hypertensive medications; (vi) the use of ambulatory blood pressure monitoring in exercise treatment; and (vii) future directions.

Before these topics can be addressed, however, definitions of the physical activity-exercise spectrum need to be established. Physical activity is any bodily movement resulting from the contraction of the skeletal muscles.^[6] Physical activity can include gardening, washing the car or cleaning the house, but should add up to a net energy expenditure of >150 kcal/day. Physical activity has been found to be effective in preventing modern chronic disease.^[6]

Exercise training is the use of more structured exercise to improve components of physical fitness (i.e. cardiorespiratory endurance, muscle strength, muscle endurance, and flexibility). Health benefits

can also be derived from exercise training.^[22] In exercise training, the mode of exercise, as well as the frequency, duration and intensity of training are critical in achieving fitness outcomes. The mode must be specific to the targeted component of fitness and the frequency, duration and intensity must be combined in a systematic overload that will result in physiological adaptations. For example, cardiorespiratory endurance can only be increased through the use of cardiorespiratory exercise (i.e. walking, swimming, jogging, cycling) that is performed more than 2 days per week, for more than 20 minutes at an effort greater than a 60% intensity.^[23]

Resistance training is the mode of exercise utilised to increase muscle endurance as well as muscle strength. Variations in the number of repetitions and in the load (% of maximal lift) determine whether the programme is targeting muscle endurance or muscle strength. Whereas a high number of repetitions (12–20) with low loads (60–80%) targets muscle endurance, a low number of repetitions (3–9) with high loads (80–90%) targets muscle strength.^[24]

Exercise treatment is the use of exercise training to prevent or treat modern chronic disease. When the term, 'exercise', is used in this review, without other descriptors such as 'training' or 'treatment', 'exercise' will be considered a comprehensive term that includes physical activity, exercise training and exercise treatment.

1. Current Research Findings in Exercise Treatment of Hypertension

It is well established that exercise can reduce high blood pressure^[3-6] following a single exercise treatment,^[25,26] a cardiorespiratory exercise training programme,^[27-33] and more recently, with physical activity.^[34] The reduction in blood pressure following a single exercise treatment is 5–8mm Hg for 11–12 hours for systolic, and 6–8mm Hg for 6–8 hours for diastolic blood pressure.^[25,26] The term,

'post-exercise hypotension', was fashioned^[15,35] to define this phenomenon of blood pressure reduction following a single exercise treatment. For a clinician, this term may be misleading. Many clinicians consider 'hypotension' to be a blood pressure that is physiologically too low. However, the researchers intended the term to reflect a 'relative', yet normal reduction in blood pressure observed following a single bout of exercise.

The reduction in blood pressure following exercise treatment ranges from 5–25mm Hg for systolic and 3–25mm Hg for diastolic blood pressure,^[15] with the average reduction for hypertensive patients to be 11mm Hg for systolic and 8mm Hg for diastolic blood pressure.^[19] However, exercise is not effective for all hypertensive adults.^[15,19] The mechanisms of blood pressure reduction through exercise treatment is also unclear.^[19,36]

Exercise has also been shown to reduce blood pressure of normotensive adults. This reduction averages 3.2mm Hg for systolic and 3.1mm Hg for diastolic blood pressure.^[16] These reductions reinforce the theory that exercise prevents hypertension.^[17,18,22,37] Because normotensive((**Author: normotensive?**)) individuals remain normotensive with exercise treatment, this review will focus on hypertensive patients.

2. The Exercise Prescription for Blood Pressure Reduction

Since 1986,^[38] the recommended exercise prescription for hypertension has developed into the following:^[36]

- mode: dynamic cardiorespiratory exercise;
- frequency: 3–5 sessions per week;
- duration: 20–60 minutes;
- intensity: 40–70% of maximal physical work capacity.

How do these variables interact to lower blood pressure?

2.1 Mode of Exercise in Hypertension

Physical activity has been well recognised as an effective means of preventing modern chronic disease, including hypertension,^[22,37] in developed

countries.^[6] However, until its role in the rehabilitation of disease is well established, considerations for the mode of exercise for the treatment of hypertension include the traditional modes that affect changes in fitness, cardiorespiratory and resistance training. Cardiorespiratory and resistance training have also been recognised as effective in the prevention of hypertension;^[17,18] however, their role in the treatment of hypertension is less definitive.

The most recent meta-analysis((**Author: meta-analyses or meta-analytic reviews?**)) of the current literature on exercise and blood pressure reduction were conducted by Kelley and Kelley for resistance training,^[18] and Whelton and colleagues^[17] and Fagard^[20] for cardiorespiratory training. Even though these reviews summarised 66 of the most well-controlled studies, limitations still exist. Only three of the 12 studies (a total of 54 study participants) utilising resistance training were conducted with hypertensive individuals,^[18] whereas 30 of the 54 studies (a total of 1214 study participants) utilising cardiorespiratory training were conducted with hypertensive individuals((**Author: please confirm that rewording is ok**)).^[17] Figure 1 is a comparison of the blood pressure reduction data from these reviews for the hypertensive individuals. Kelley and Kelley^[18] reported resistance exercise to be as effective as cardiorespiratory exercise in reducing high

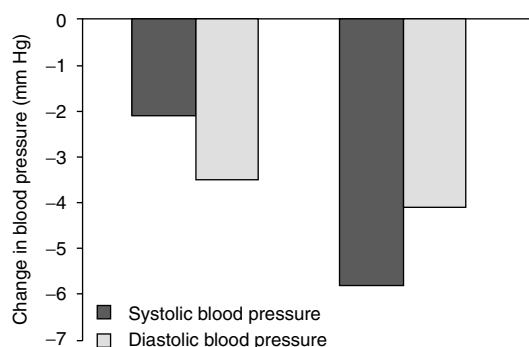


Fig. 1. A comparison of blood pressure reduction between cardiorespiratory and resistance exercise training (reproduced from Whelton et al.,^[17] and Kelley and Kelley^[18])(**Author: with permission? Please provide a copy of the permission letter from the publisher and the author if this has been reproduced or modified from another publication. Also, please provide x-axis labels**)

blood pressure; however, further inspection may not support these conclusions.

Although the resistance training groups for hypertensive individuals reduced blood pressure by an average of $-2.1/-3.5$ mm Hg following the treatment ((Author: exercise treatment?)), the blood pressure change in the control groups was not different; $-2.1/-2.3$ mm Hg for systolic and diastolic pressures, respectively. Because the changes associated with resistance training cannot be attributed to that training when the control groups exhibit the same response, the conclusion that resistance exercise reduces high blood pressure in hypertensive adults is suspect. Reviews by both Tipton^[15] and Fagard and Tipton^[16] reported the only resistance exercise studies found to decrease blood pressure were those that combined resistance with cardiorespiratory endurance exercise. Resistance programmes alone did not lower blood pressure.

In the past, resistance exercise had been considered a contraindication for hypertensive patients because of the excessive pressor load it puts on the heart. However, a significance of the reviews by Kelley and Kelley^[18] and others^[15,16,30] is that resistance training does not exacerbate blood pressure and is not associated with precipitating cardiac events.^[36] Resistance exercise should not be the primary mode of exercise for the reduction of high blood pressure.^[36] However, if resistance training is essential to improve activities of daily living, it should not be excluded from exercise therapy in hypertension. Resistance exercise most likely needs to be modified to be safe and effective in hypertension. The safety of resistance exercise can be accomplished by prescribing programmes designed for muscle endurance rather than for muscle strength, and by monitoring diastolic blood pressure during the exercise.

Even low intensity static exercise can result in elevated diastolic blood pressures.^[39] The actual diastolic blood pressure response to resistance exercise depends on how much static work is integrated into the movement. Most programmes will establish termination points for resistance exercise based on the diastolic blood pressure. These limits have typically been an absolute increase in diastolic pressure

of >20 mm Hg above rest or a diastolic blood pressure of ≥ 120 mm Hg.^[40] However, reaching these diastolic pressures during resistance work does not necessitate avoidance of resistance exercise. The resistance exercise can simply be modified.

Figure 2 illustrates an algorithm for the use of resistance exercise in the treatment of hypertension. To start, measure the diastolic blood pressure response to the prescribed resistance programme. If the diastolic pressure remains within the guidelines, continue with that programme. However, if the diastolic blood pressure is too high, increase the repetitions and/or decrease the resistance. Continue monitoring the diastolic blood pressure after adjusting the repetitions/load. If the modifications result in a desirable diastolic blood pressure response, continue with this modified exercise programme. However, if the modification of the repetitions/load does not bring the diastolic blood pressure response low enough, a reduction in the number of upper body resistance exercises and/or an increase in the number of lower body resistance exercises may be more

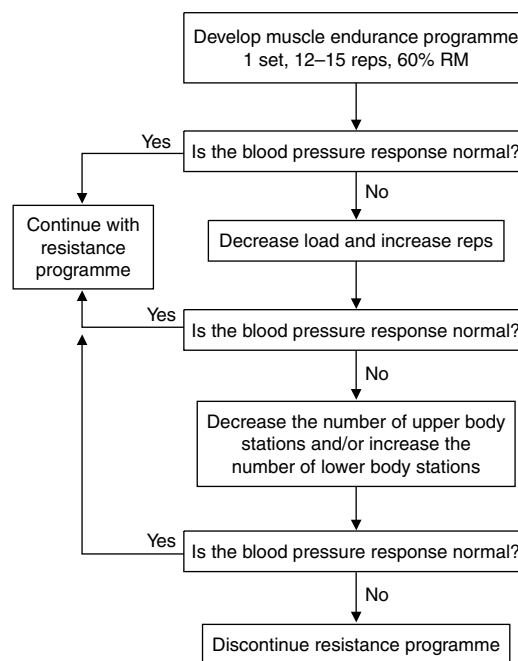


Fig. 2. Algorithm for the management of blood pressure during resistance exercise. **reps** = repetitions; **RM** = repetition maximum.

effective. Continue monitoring the diastolic blood pressure after adjusting the upper/lower body exercises. If the blood pressure response is desirable, continue with this exercise programme. However, if the diastolic pressure continues to increase too high despite these modifications, resistance exercise does become a contraindication for that individual patient.

Monitoring diastolic blood pressure during resistance exercise should be at the beginning of a resistance programme or when modifications are made to the resistance programme. To monitor the diastolic blood pressure during exercise, have the patient exercise while wearing a blood pressure cuff (**Author: please confirm that rewording is ok**). Pump the cuff up during the last few repetitions, if possible, or immediately after the exercise has been completed. Release the pressure on the cuff and measure the blood pressure. Continue this sequence for each resistance station. Different modifications in load and repetitions are possible for each resistance station.

The American College of Sports Medicine recommends resistance exercise in the form of circuit training.^[36] Kelley and Kelley reported greater blood pressure reductions in resistance exercise that utilised circuit training rather than traditional strength training.^[18] Circuit training is characterised by lighter loads and more repetitions whereas traditional strength training utilises higher loads and fewer repetitions.

The haemodynamic response to cardiorespiratory versus resistance exercise may illustrate why cardiorespiratory exercise is more efficient in reducing high blood pressure. Cardiorespiratory endurance exercise places a volume load on the heart whereas resistance exercise places a pressure load on the heart. When measuring the blood pressure with auscultation, the normal blood pressure response to a cardiorespiratory stimulus is an increase in systolic pressure, proportional to the effort, with either no change or a slight decrease in diastolic pressure. Whereas the normal blood pressure response to resistance exercise is a pressor response for both sys-

tolic and diastolic pressures, proportional to the muscle mass and the effort.

In summary, cardiovascular exercise is the preferred mode for the exercise treatment of hypertension. Resistance exercise is not recommended as the primary mode, but can be prescribed in the form of muscle endurance. Resistance exercise should be monitored in the beginning of a programme or when changes are made to a programme to assure a safe diastolic blood pressure response.

2.2 Frequency and Duration of Exercise in Hypertension

Although frequencies ranging from 1–7 days per week have been utilised in blood pressure reduction for hypertensive studies, the number of studies investigating the influence of frequency and duration of exercise on blood pressure reduction in hypertension have been limited.^[41–44] Whelton and colleagues reported no influence of frequency of exercise on the blood pressure reduction in their meta-analytical review.^[17] However, they reported frequencies in ‘minutes per week’, which is more a measure of duration than frequency. Figure 3 illustrates the relationship between frequency of exercise and the change in blood pressure for the 30 randomised, controlled, clinical trials that Whelton and colleagues^[17] identified for hypertensive individuals. This relationship is not strong, perhaps because the other exercise variables of duration and frequency were not controlled. Even though blood pressure reductions were found for 1^[45] and 2^[46] days per week, a frequency of 3 days per week has been considered to be the minimal frequency for blood pressure reduction.^[36] Higher frequencies tended to produce greater reductions, although not significantly different. If a weight loss is desired, a higher frequency, up to five (**Author: days?**) per week, will optimise weight loss.^[40]

The range of exercise duration reported in the literature has been 10–60 minutes. Similar to frequency of exercise, the duration of exercise has not been the main focus of investigation.^[41,43] Figure 4 illustrates the relationship between duration of exercise and the change in blood pressure for the 30

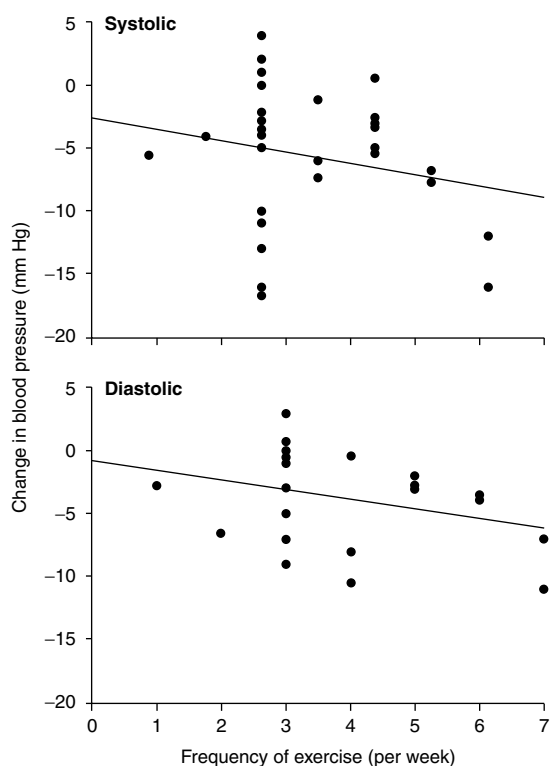


Fig. 3. The relationship between frequency of exercise and the change in blood pressure in randomised, controlled, clinical trials using patients with hypertension (reproduced from Whelton et al.^[17]). **((Author: with permission? Please provide a copy of the permission letter from the publisher and the author if this has been reproduced or modified from another publication. Also, should the x-axis label be changed to 'Frequency of exercise (sessions per week)'?))**

randomised, controlled, clinical trials that Whelton and colleagues^[17] identified for hypertensive individuals. The relationship between duration and blood pressure reduction is not strong, similar to the relationship between frequency and blood pressure reduction. MacDonald and colleagues^[43] reported that a duration of exercise as short as 10 minutes can result in a significant blood pressure reduction. Longer durations appear to produce greater blood pressure reductions, although not significantly different. Once again, however, the interaction of the other exercise variables was not controlled.

No study exists utilising a systematic control of exercise frequency, duration, and intensity except for a single exercise treatment.^[41] The data from our

laboratory suggest that longer exercise duration may be more effective than shorter duration. In this study, the blood pressure reduction for 27 borderline hypertensive adults was compared among four treatment groups and a non-exercise control group. The treatment groups varied in intensity (50 or 70% of maximum oxygen uptake [$\dot{V}O_{2max}$]) and duration (15 or 45 minutes). Frequency was controlled because the treatment was a single exercise bout. The 50%/45-minute group demonstrated the largest reduction in blood pressure following exercise (figure 5).

Until a systematic approach to investigating frequency and duration of exercise, while controlling for the other exercise variables is accomplished, the influence of frequency and duration on blood pres-

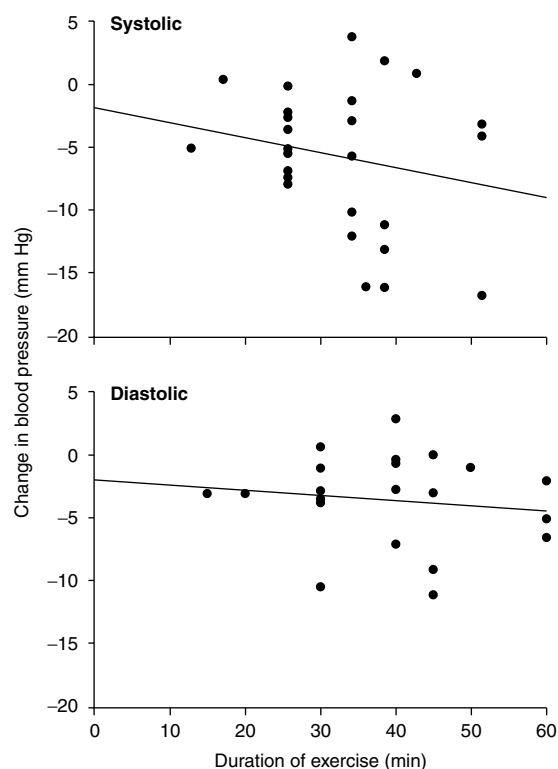


Fig. 4. The relationship between duration of exercise and the change in blood pressure in randomised, controlled, clinical trials using patients with hypertension (reproduced from Whelton et al.^[17]). **((Author: with permission? Please provide a copy of the permission letter from the publisher and the author if this has been reproduced or modified from another publication))**

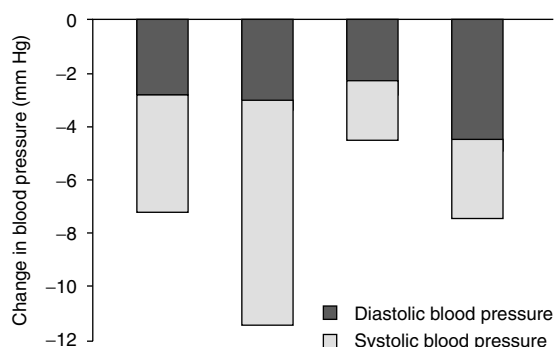


Fig. 5. The influence of exercise intensity on blood pressure reduction following exercise (reproduced from Inbar et al.,^[41]). **(Author: with permission? Please provide a copy of the permission letter from the publisher and the author if this has been reproduced or modified from another publication. Also, please provide x-axis labels and check that this is the correct figure legend)**

sure reduction remains unclear. It is possible that different frequencies and durations may be suited to different subgroups of hypertensive patients.

2.3 Intensity of Exercise in Hypertension

The range of exercise intensity reported in the literature has been 40–85% $\dot{V}O_{2max}$. Even though the intensity of exercise has been investigated more than the other exercise variables of frequency and duration,^[20,32,41,47-51] more disagreement exists now regarding the most effective exercise intensity for blood pressure reduction in hypertension.

In the past, Hagberg et al.^[47] and Tipton et al.^[52] reported lower intensities to be more effective than higher intensities in lowering high blood pressure. In fact, higher intensity exercise was considered to exacerbate hypertension.^[36,47,52] In a 1994 review by Fagard and Tipton^[16] of the 36 well-controlled studies, those investigators who utilised intensities below 70% $\dot{V}O_{2max}$, exhibited a significant reduction in systolic and diastolic blood pressure ($\downarrow 6.8/4.4$ mm Hg), whereas those investigators who utilised intensities above 75% $\dot{V}O_{2max}$ found either no change or an increase in blood pressure with exercise ($\uparrow 3/\downarrow 1$ mm Hg). Hagberg, in his most recent review, reported current studies continued to support the lower intensity (<70% $\dot{V}O_{2max}$) exercise as more effective than high intensity (>70% $\dot{V}O_{2max}$) exer-

cise.^[19] Therefore, it appeared as though intensities over 75–80% $\dot{V}O_{2max}$ may not be effective, and in some cases appear to exacerbate hypertension.^[19,47,52]

On the other hand, in the more recent meta-analytic reviews by Whelton and colleagues^[17] and Fagard,^[20] both reported no influence of exercise intensity on blood pressure reduction following exercise treatment. Figure 6 illustrates the relationship between intensity of exercise and the change in blood pressure for the 30 randomised studies that Whelton and colleagues^[17] identified for hypertensive individuals. This relationship is less strong than the duration and frequency of exercise. Whelton did not control for the other exercise variables of dura-

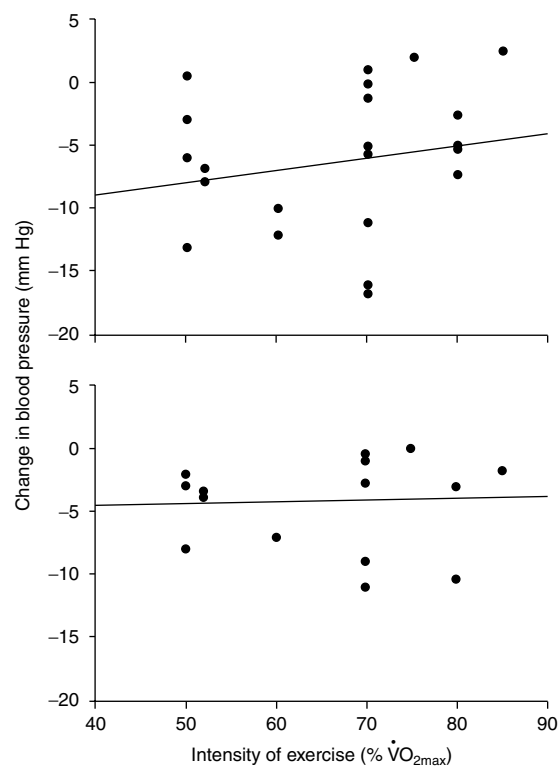


Fig. 6. The relationship between intensity of exercise and the change in blood pressure in randomised, controlled, clinical trials using patients with hypertension (reproduced from Whelton et al.,^[17] $\dot{V}O_{2max}$ = maximum oxygen uptake). **(Author: with permission? Please provide a copy of the permission letter from the publisher and the author if this has been reproduced or modified from another publication)**

tion and frequency when observing the influence of exercise intensity. Later, when Fagard analysed six focused studies that compared the effects of more than one exercise intensity on blood pressure reduction,^[32,47-51] no effect of exercise intensity was reported.^[20] However, the low and high intensities used for Fagard's review were $40.2 \pm 2.3\%$ $\dot{V}O_{2\max}$ and $68.5 \pm 3.3\%$ $\dot{V}O_{2\max}$, respectively. The studies that utilised higher exercise intensities $>75\%$ $\dot{V}O_{2\max}$ were not included in Fagard's comparison. Consequently, these two most recent reviews do not contradict the earlier statements that low intensity exercise is more effective than high intensity exercise in blood pressure reduction; Whelton and colleagues by not controlling for the other variables, and Fagard for not reviewing studies with higher intensities. Until more well-controlled studies utilising the range of exercise intensity, while controlling for the other exercise variables can be undertaken, the critical exercise intensities for blood pressure reduction remains less definitive.

3. The Interaction of Bodyweight, Hypertension and Blood Pressure Reduction

Excess body fat,^[53] especially upper body fat,^[54-57] has been associated with increased incidence of hypertension. Consequently, weight loss is recommended as an effective non-pharmacological means of reducing blood pressure.^[7] Several reviewers agree that the reductions in blood pressure found in exercise treatment have been independent of bodyweight or body fat changes.^[17,19,36] Therefore, exercise probably does not reduce blood pressure through a weight loss mechanism and exercise can be effective in blood pressure reduction without changes in bodyweight. When exercise is combined with diet to reduce bodyweight or body fat, there also appears to be no additive effect.^[58,59] However, if weight loss is desired, the combination of diet and exercise is the most effective means of weight reduction and maintenance.^[60]

4. Who Benefits from the Exercise Treatment of Hypertension?

Bouchard and Rankinen,^[61] in a study designed to investigate the role of genetics in risk factor reduction through exercise intervention, reported considerable heterogeneity in the responsiveness to regular physical activity. The literature that is focused on the exercise intervention of hypertension is not different. **((Author: please confirm that rewording is ok))** Approximately 75% of hypertensive patients who exercise will reduce blood pressure with exercise treatment.^[19] Even so, the blood pressure reduction varies within these responders:^[12,15,16,19,62-64]

- women may reduce blood pressure more than men;^[19]
- Asian and Pacific Islanders have a greater reduction in blood pressure than Caucasians;^[19]
- hypertensive individuals with high sodium (Na) to potassium (K) ratio lower blood pressure more than those with low Na : K ratios;^[62]
- hypertensive adults with low peripheral vascular resistance exhibit a greater reduction than high peripheral vascular resistance;^[62,64]
- borderline hypertensive patients may be more successful than patients with essential hypertension;^[12,15]
- hypertensive patients with higher blood pressures may reduce blood pressure more than those with more borderline or normal pressures;^[16,63]
- the blood pressure reduction of hypertensive patients taking non-selective **((Author: β?))-blockade** may be compromised compared with hypertensive patients taking other types of anti-hypertensive medications (see comments in section 5).^[65]

Finally, Nami and colleagues identified nocturnal non-dippers as non-responders to exercise treatment for hypertension.^[66] Nocturnal non-dippers are defined as hypertensive adults whose night-time (2200–0600 hours) blood pressure does not fall $>10\%$ below the day-time (0600–2200 hours) blood pressures. Data in our laboratory do not support the findings of Nami and colleagues (see comments in section 6).

The variation in blood pressure reduction, including the non-responders, may be due to pathophysiology of the disease and/or due to genetic differences. For example, haemodynamic variables are pathological variations of the disease and have been identified among the characteristics of low- and non-responders.^[62]

When the haemodynamics of elevated blood pressure were investigated in response to exercise treatment, a decrease in cardiac output,^[67-69] a decrease in peripheral vascular resistance,^[70] decreases in both,^[67] and no change in either^[28-30,44,62,71-73] have been reported. Kinoshita and colleagues,^(Author: reference^[62] ?) as well as studies in our laboratory,^[64,74] demonstrate that the reduction in cardiac index is more likely for a hypertensive patient who presents with an elevated cardiac index. Similarly, a reduction in peripheral vascular resistance may be more likely for a patient who presents with an elevated peripheral vascular resistance. Perhaps the other characteristics of low- and non-responders need to be targeted in the exercise treatment before reductions can be observed. However, the field has failed to develop a systematic observation of the effects of exercise treatment on different variations in hypertensive pathophysiology.

Bouchard and Rankinen found the heterogeneity of blood pressure responses to exercise treatment not to be random, but to be related to familial aggregation.^[61] Genome identification^[75-78] and genotype^[79] for blood pressure reduction through exercise intervention has been the focus of recent investigations. In the HERITAGE Family Study, the blood pressure response to exercise training was investigated in 519 Caucasian individuals from 98 families and 317 African-American individuals from 114 families following 20 weeks of endurance training.^[80] The genome links to blood pressure reduction were identified in three regions.^[75-77] Hagberg and colleagues observed the blood pressure responses to 9 months of exercise treatment for 18 individuals identified to have three genotypes of angiotensin converting enzyme (ACE).^[79] Significant reductions in blood pressure were found for

two the genotypes, but not for the third. Therefore, genetic variations may account for some of the differences in blood pressure reduction through exercise.

In summary, the response to exercise training is variable. Characteristics of responders and non-responders have been identified and may be influenced by pathology of hypertension and/or genetics. Further research is needed on both of these fronts. Perhaps there may be more than one optimal exercise prescription for the hypertensive patient who is currently identified as a low- or non-responder.

5. The Interaction of Exercise and Anti-Hypertensive Medications

Both cardiorespiratory exercise and anti-hypertensive medications effectively reduce blood pressure. If exercise is combined with antihypertensive medication, will the resultant reduction in blood pressure be additive? Are there any anti-hypertensive medications that compromise exercise effectiveness?

Keleman and colleagues,^[81] and Stewart and colleagues^[82] ((Author: please confirm that rewording is ok)) randomised 51 hypertensive patients into three anti-hypertensive medication groups (placebo, propranolol, diltiazem) in a double-blind design. All patients were exercised for 10 weeks in circuit training and aerobics. All three groups exhibited a significant reduction in blood pressure, none, of which, was significantly different from the other.^[81] Thus, it appears as though the actions of anti-hypertensive medications and exercise are not additive. On the other hand, exercise performance was compromised in the propranolol group.^[82]

It is well known that β -blockade((Author: Please confirm that this should be a ' β ' symbol throughout the article? It appeared as a back-to-front E in the electronic file you originally sent to us.)) compromises exercise performance in non-cardiac patients, but improves exercise performance in cardiac patients limited by ischaemia.^[83] The cardioselectivity and intrinsic sympathomimetic activity (ISA) properties of β -blockade((Author: Again, β symbol correct here?)) may also play a

role in exercise effectiveness. Duncan and colleagues^[84] randomised 50 hypertensive adults into placebo, propranolol (no ISA), and pindolol (ISA) groups for a 22-week double-blind exercise study. Medications were titrated to produce blood pressures <140/90mm Hg before training began. Similar to the findings of Keleman and colleagues,^[81] there was no difference in the reduction of blood pressure among the three groups. However, the two groups taking β -blockade ((Author: β correct?)), during the titration phase, exhibited a decreased exercise performance that increased slightly with training, but not significantly greater than before drug treatment.

In a similar design, Gordon and Duncan^[83] observed the characteristics of exercise performance among placebo, propranolol (non-selective), and atenolol (β_1 selective) ((Author: Please confirm β symbol is the correct symbol to appear throughout the rest of this section)) groups. $\dot{V}O_{2\max}$ and endurance time were lowest in the propranolol group, low in the atenolol group, and normal in the placebo group. In addition, β -blockade may compromise thermoregulation during exercise^[83] as well as attenuate the exercise effectiveness on lowering lipids.^[84]

β -blockade has not been the medication of choice for combining exercise with anti-hypertensive medications in the treatment of hypertension.^[36,81-85] However, if β -blockade is to be prescribed, β_1 selective blockers are the preferred β -blocker for use with patients who exercise.^[83]

ACE inhibitors, calcium channel blockers and central α -agonists exhibit the least adverse effects on exercise.^[85] Pool and colleagues,^[86] reported that diltiazem may be more advantageous in lowering blood pressure, lowering blood lipids, and improving exercise performance than β -blockers or diuretics. Diuretics have few deleterious effects on exercise performance,^[85] except when potassium is depleted. Exercise may exacerbate fatal dysrhythmia in hypokalaemia.^[40]

6. The Use of Ambulatory Blood Pressure Monitoring in Exercise

Ambulatory blood pressure monitoring has had limited use in exercise studies.^[26,29,31,33,63,66,68,87-90] Ambulatory monitoring has been used effectively to determine the most effective pharmacological dosage for hypertension^[91] because it has been found to: (i) increase sensitivity compared with clinical measures; (ii) improve accuracy compared with clinical measures; and (iii) represent the blood pressures of activities of daily living.^[92] ((Author: please confirm that rewording is ok)) Ambulatory technology can use the same way to determine the most

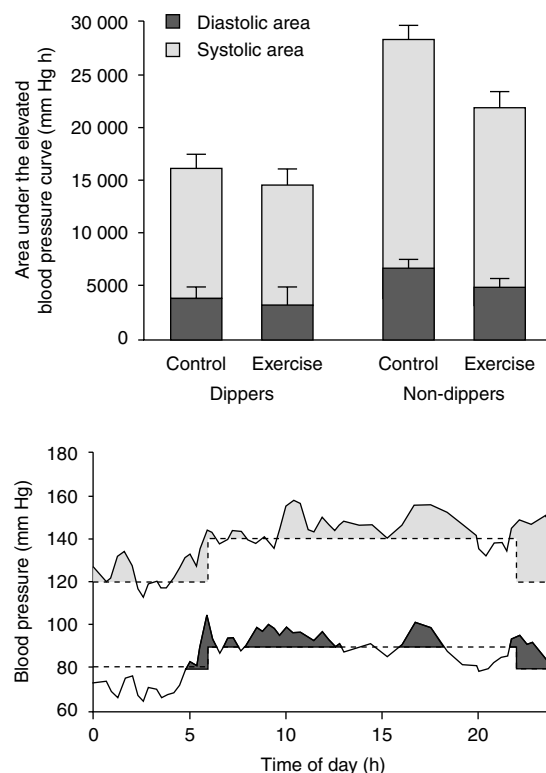


Fig. 7. Ambulatory blood pressure reduction following exercise in nocturnal dipping and non-dipping hypertension. Panel B illustrates the area under the elevated blood pressure curve for 24-hour average pressure = 139/88mm Hg. Criteria for day-time and night-time elevations are 140/90mm Hg and 120/80mm Hg (reproduced from Wallace et al.^[96]). ((Author: with permission? Please provide a copy of the permission letter from the publisher and the author if this has been reproduced or modified from another publication))

effective exercise dose for the low- or non-responsive patients.

In the analysis of ambulatory blood pressure data, the measurements of diurnal variation provide information beyond the simple variables that reflect the quantity of hypertension (i.e. average 24-hour pressures, blood pressure loads, and area above the elevated blood pressure curve). With advanced ambulatory blood pressure data analysis, critical periods of blood pressure elevation such as the character of the nocturnal blood pressure^[93] as well as the morning rise systolic blood pressure^[94] can be observed in response to treatment, whether the treatment is pharmacological or exercise.

For example, utilising these techniques in our laboratory we found that the nocturnal non-dipper, previously defined as a non-responder,^[66] may not be a non-responder after all.^[95-97] Figure 7 and figure 8 illustrate the results of a series of studies in our laboratory to find an optimal exercise treatment for non-dipping hypertensive adults. First, non-dippers ($n = 14$; day-time systolic blood pressure = 149.2 ± 12.6 mm Hg; and night-time systolic blood pressure = 142.5 ± 14.3 mm Hg) were found to respond to exercise treatment not only with reductions in 24-hour average systolic blood pressure ($-5.1 + 1.1$ mm Hg ((Author: $\pm?$))), but reductions in day-time ($-4.3 + 0.9$ ((Author: $\pm?$))) and night-time ($-9.9 + 3.9$ mm Hg ((Author: $\pm?$))) blood pressures as well.^[95] In fact, the night-time systolic blood pressure reduction was greater than the day-time blood pressure reduction. Figure 7 illustrates non-dippers ($n = 20$; day-time = $149.5 \pm 8.5/89.0 \pm 9.2$ mm Hg; and night-time = $144.7 \pm 12.0/87.3 \pm 14.0$ mm Hg) respond similarly as dippers ($n = 24$; day-time = $146.9 \pm 10.2/88.7 \pm 5.8$ mm Hg; night-time = $123.1 \pm 11.1/73.7 \pm 11.9$ mm Hg) to a single exercise (50 minutes at $50\% \dot{V}O_{2max}$) treatment.^[96] Because a single exercise treatment lowers blood pressure for 5–8 mm Hg for 11–12 hours for systolic and 6–8 mm Hg for 6–8 hours for diastolic blood pressure,^[25,26] a sub-group of five non-dippers (24 hours = $152.2 \pm 3.8/83.0 \pm 5.4$ mm Hg; day-time = $152.2 \pm 5.1/84.0 \pm 4.8$ mm Hg; and night-time = $151.0 \pm 8.8/78.0 \pm 10.0$ mm Hg) were given morning

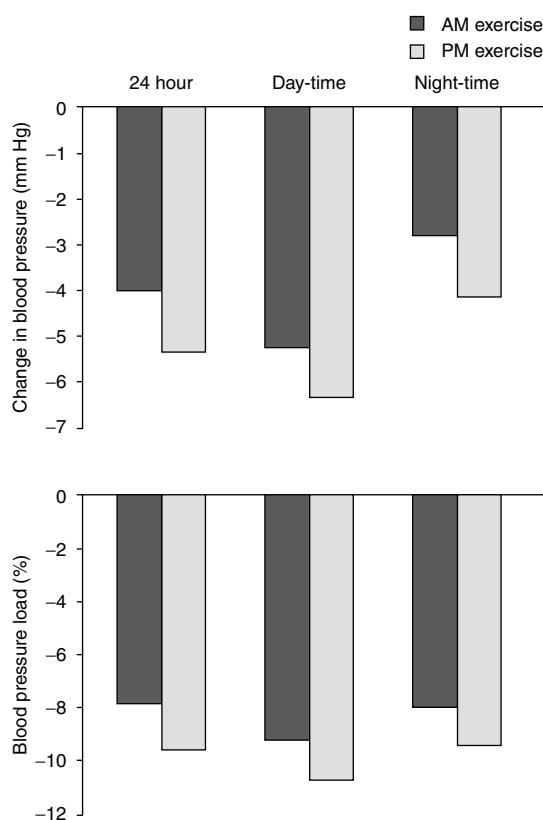


Fig. 8. Ambulatory blood pressure reduction following morning (AM) and evening (PM) exercise treatment in nocturnal non-dipping hypertension. (reproduced from Park et al.,^[97] ((Author: with permission? Please provide a copy of the permission letter from the publisher and the author if this has been reproduced or modified from another publication)))

and evening exercise (40 minutes at $50\% \dot{V}O_{2max}$) and control treatments, in a randomised design.^[97] It was anticipated that the evening exercise treatment would be more effective in lowering the blood pressure of the non-dippers, since the night-time elevations of the non-dippers remains characteristically high. Figure 8 illustrates that evening exercise is more effective than morning exercise in reducing blood pressure for non-dipping hypertensive adults.

In summary, ambulatory blood pressure monitoring provides additional means of analysing the blood pressure responses to exercise. The utilisation of the ambulatory blood pressure technology cannot only recategorise previously identified non-respon-

ers, but can be used to find the most effective exercise dose for subpopulations.

7. Future Directions

((Author: please add a conclusions paragraph here. This section should summarise the main findings of the article and draw conclusions. The section should then be retitled Conclusions and Future Directions))

The study of effectiveness of exercise in the treatment of hypertension is unfinished. Although it is well established that cardiovascular exercise training is the most effective mode of exercise in the prevention and treatment of hypertension, not all hypertensive patients respond to exercise treatment. Two areas of research can be identified to solve the same problem. Differences to the response to exercise may not only be found in genetics and pathophysiology, but may also be found in the exercise prescription itself. The tools now exist to further investigate the optimal exercise dose for low- and non-responders. Observation of the ambulatory blood pressure response following modifications of single exercise treatments can be an effective means to find the exercise dose that may be more effective for a specific population.

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