

31. Hypertension

Authors

Mats Börjesson, MD, PhD, Associate Professor, Department of Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden

Sverre Kjeldsen, MD, PhD, Professor, Department of Cardiology, Oslo University Hospital, Ullevål, Norway

Björn Dahlöf, MD, PhD, Associate Professor, Department of Medicine, Sahlgrenska University Hospital Östra, Gothenburg, Sweden

Summary

Hypertension, that is, above-normal blood pressure, is the most important, modifiable risk factor for cardiovascular disease and mortality. The incidence is increasing in most countries and lifestyle factors are considered to play a decisive role in this development. Obesity, physical inactivity and increased salt intake, in particular, have varying degrees of significance in different populations. As a single risk factor, physical inactivity is believed to be responsible for 5–13 per cent of hypertension today.

Most cases of hypertension are currently still undetected, untreated and/or have not reached therapeutic target value for treatment. This leaves much room for improved treatment, both via an increase in non-pharmacological treatment and via different pharmacological options.

Available data from a recent meta-analysis shows that aerobic fitness training lowers blood pressure approximately 7/5 mmHg in people with mild to moderate hypertension. A single episode of physical activity yields an acute lowering of the blood pressure, so-called post-exercise hypotension. Repeated sessions of physical activity are therefore a strategy for lowering blood pressure, but to attain a lasting reduction of pressure regular exercise is required.

Type of exercise training	Prescription
Aerobic fitness training	40–70 per cent of individual maximal oxygen uptake capacity 5–7 days/week, a minimum of 30 minutes per training session
Strength training	many repetitions and low resistance

Dividing the activity, for example, into 4 sets of 10-minute sessions, can be just as effective as a single 40-minute dose of training per day.

Introduction

Hypertension, or more correctly blood pressure that is too high, is defined as a systolic pressure of ≥ 140 mm Hg and/or a diastolic pressure of ≥ 90 mm Hg, on repeated measurements under standardised conditions (1). In certain high-risk individuals, such as patients with diabetes or kidney disease, the target level for blood pressure treatment is even lower (1).

Hypertension is a significant independent risk factor for cardiovascular disease and the most important modifiable cause of mortality (1). More than 7 million deaths per year across the world are due to hypertension (2). Different national and international organisations have defined the concept of “hypertension” and also divided the disease into degrees of severity based on a number of large epidemiological and treatment studies. The most recently published European guidelines give the following classifications of hypertension (1):

Table 1. Classification of hypertension.

	Systolic	Diastolic
Optimal blood pressure	< 120	< 80
Normal blood pressure	< 130	< 85
High normal blood pressure	130–139	85–89
Grade 1 hypertension (mild)	140–159	90–99
Grade 2 hypertension (moderate)	160–179	100–109
Grade 3 hypertension (severe)	≥ 180	≥ 110
Isolated systolic HT	≥ 140	< 90

It is estimated that at least 25 per cent of the Swedish population (increases with age) suffer from hypertension or take antihypertensive drugs. Globally, the number of people with hypertension is growing dramatically and is estimated to reach close to 1.6 billion people, or 30 per cent of the world’s population by 2025 (3, 4).

Ninety-five per cent of all hypertension is called “essential”, that is, where no single identifiable cause can be shown (1, 5). Essential hypertension is probably the product of many factors that interact in a complex manner in the development of high blood pressure, including genetic factors, environmental factors such as diet, physical inactivity and stress, and psychosocial factors (1, 5). Over the past decades, changes in lifestyle for the worse have been decisive for the increased incidence of hypertension and cardiovascular disease, which is especially pronounced in the developing countries (2). Obesity, physical inactivity and increased salt intake are specific factors of varying importance in different populations, where physical inactivity alone is estimated to represent 5–13 per cent of the risk of developing hypertension (6).

The remaining 5 per cent of people with hypertension suffer from secondary hypertension resulting from, for example, renovascular disease (e.g. renal arterial stenosis), Cushing’s syndrome, pheochromocytoma or coarctation of the aorta. These types of secondary hypertension are best addressed through possible correction of the underlying cause.

Simplified, blood pressure is the result of cardiac output multiplied by the peripheral resistance ($BP = CO \times PR$). In the development of hypertension, there is usually an initial increase in cardiac output, which is a product of heart rate and the heart's stroke volume. An increased resistance gradually develops peripherally in the vascular bed, which in turn leads to secondary, more manifest vascular changes (a vicious circle). At this point, the elevation in blood pressure becomes more established and more resistant to treatment.

Risks of high blood pressure

Untreated, high blood pressure leads to secondary vascular changes consisting of a thickening of the blood vessel walls, impaired endothelium function, and atherosclerosis of the large and medium-sized arteries. In addition, left ventricular hypertrophy of the heart and/or albumin leakage in the kidneys, proteinuria, are seen, and are in themselves also associated with increased mortality and morbidity (1, 7, 8). In order for atherosclerosis to develop, high blood pressure must be present: in the venous low pressure system, for example, atherosclerosis never occurs, while if veins are moved to the arterial system (e.g. via bypass grafting in coronary artery surgery) atherosclerosis develops in a matter of months.

The risk for fatal and non-fatal cardiovascular complications (especially coronary artery disease and stroke), kidney disease and other heart and vascular complications increases parallel to increases in both systolic and diastolic blood pressure levels (8).

Advantages of treating high blood pressure

Pharmacological treatment of hypertension has a long, well-established history. Successful lowering of blood pressure yields fewer cardiovascular events parallel to the degree of blood pressure-lowering (1). According to a meta-analysis of 61 studies covering a million individuals, we can expect a 7 per cent reduction in coronary artery disease and 10 per cent reduction in stroke for every 2 mmHg reduction in blood pressure (8). This is especially important in light of the fact that most cases of hypertension today are still undetected, untreated and/or have not yet reached the appropriate treatment target value (1, 9, 10). There is thus much room for improved treatment via both pharmacological and non-pharmacological methods.

Although there is a lack of formal mortality and morbidity studies with respect to effects of physical activity on high blood pressure, it is well-documented that better fitness/higher levels of physical activity are associated with lower mortality in hypertensives (11), as in non-hypertensive people (12). Recent findings from the LIFE study (Losartan versus Atenolol-based therapy for patients with hypertension and left ventricular hypertrophy) report increased physical activity to be associated with fewer complications, independent of treatment (13).

Effects of physical activity on blood pressure

A single episode of physical activity yields an acute lowering of the blood pressure, so-called post-exercise hypotension. Repeated bouts of physical activity are therefore a strategy for lowering blood pressure (14). This acute effect of increased activity is, however, not the whole truth, as physical activity also has a more lasting effect. These different effects of physical activity are mediated by different mechanisms.

Acute effects

Aerobic fitness training

During dynamic physical activity in healthy persons, such as running, systolic blood pressure normally rises during the exercise itself. In people with hypertension, the elevation in blood pressure can be more pronounced (15). The diastolic pressure remains the same or increases slightly during exertion, mainly due to reduced vasodilating capacity (15).

After dynamic physical activity, the blood pressure falls by about 10–20 mmHg for the next few hours, compared to the person's normal resting blood pressure. This effect is called *post-exercise hypotension*. How long this lowered blood pressure lasts (up to almost 24 hours) after the exercise seems to depend on factors such as the duration and intensity of the physical activity, and whether the activity was continuous or not (16, 17). The same total physical activity, divided into smaller sessions, had a greater pressure-lowering effect than one long session (16, 17). It is believed that the blood pressure-lowering in the 24 hours following physical activity is mediated mainly via a transient reduction in stroke volume (15) and/or modulation of the sympathetic nervous tone.

Strength training/Heavy static training

When it comes to heavy static training (strength training with heavy weights), there is a stronger increase in systolic and diastolic blood pressure during the training itself, than in dynamic exercise. One typically sees a moderate increase in heart rate and cardiac output, combined with an increased in peripheral resistance (18).

Circuit training

According to a new meta-analysis of 9 short-term studies covering 341 individuals, strength training can reduce both systolic and diastolic blood pressure by approximately 3–4 mmHg (19). These studies concluded that moderate intensity strength training is not contraindicated in hypertension, and can even lead to a lowering of blood pressure, although more studies are needed with respect to the long-term effects (19). Circuit training in particular, that is, strength training of large muscle groups with lighter load and more repetitions, appears to be able to lower blood pressure (18) in addition to the positive effect on other risk factors such as insulin resistance.

Qi gong

One small study found an equivalent blood pressure-lowering effect from qi gong as compared to traditional aerobic exercise training (20). Qi gong may therefore constitute an alternative form of exercise for people with hypertension, though possible long-term effects are at present unknown and further studies are needed to confirm these initial findings.

Long-term effects

A recent meta-analysis looking at 72 studies shows that dynamic endurance training lowers blood pressure by approximately 7/5 mmHg (21) in people with mild to moderate essential hypertension. The blood pressure-lowering effect of physical activity is, not surprisingly, highest in people with established hypertension compared to those with normal blood pressure (2/2 mmHg (21)). The effects appear to be the same in people taking antihypertensive drugs (12). The blood pressure-lowering effect of dynamic training is not lasting and requires continually maintained regular activity in order to remain.

Regular physical activity not only lowers the resting blood pressure, but also decreases the blood pressure response during both physical exertion (22) and mental stress (23).

The effects usually apply regardless of age, gender and ethnicity (24). The blood pressure-lowering effect may even be stronger in African-Americans (24).

It has been suggested that the reduction in blood pressure was lower in older individuals, who have often had suffered from hypertension for a longer time and can thus be expected to have more established vascular changes. One study seems to confirm this, by showing that 6 months of exercise training produced lower diastolic- but not systolic blood pressure in people 55–75 years, while no measurable improvement in aorta stiffness was seen (25). On the other hand, a Taiwanese study showed that, in hypertensives 60 years and older, systolic blood pressure was reduced significantly more than in a control group in a 6-month walking intervention (26). Also, Fagard and Cornelissen's meta-analysis did not show any reduced efficacy of physical activity in older hypertensive patients (21).

Indications

Physical activity as primary prevention

A number of longitudinal and cross-sectional studies support a relation between low physical activity and an increased risk for developing hypertension (27). It was recently shown that being physically active during leisure time is associated with a lower risk for developing hypertension, independent of the level of physical activity at work or during transit/commuting to and from work (28).

A primary preventive study observed a 50 per cent reduction in development of hypertension development in patients at risk for hypertension aged 30–44 years: 8.8 per cent (compared to 19.2%) of those who increased physical activity and modified their diet developed hypertension in a 5-year period (29). One group with an increased risk for

coronary disease reduced their coronary risk profile to the same level as those with a low genetic risk through regular physical activity (30). To sum up, regular physical activity appears to protect against development of hypertension and reduces the elevation of pressure in predisposed individuals (31).

Predicting hypertension

Older studies have suggested that individuals with a genetic susceptibility to hypertension, but with normal blood pressure, have an exaggerated blood pressure response to dynamic and isometric exercise compared to controls without an inherited susceptibility. Longitudinal studies indicate a 2–3 times higher risk for later development of hypertension in patients with normal blood pressure who show increased elevation of blood pressure in an exercise test (34). The blood pressure after a stress test also predicts future risk (35). It is likely that the individual clinical prediction of risk for cardiovascular disease could improve if one also took into account these results from a stress test (36).

If one knows that a healthy person has an abnormal blood pressure response in a stress test, the person should be informed of an increased risk for later development of hypertension and be given appropriate advice concerning lifestyle modifications and regular blood pressure check-ups.

Treatment of hypertension/Secondary prevention of cardiovascular disease

The latest European recommendations emphasise that the increase in risk with respect to mortality is greater in people with hypertension with signs of organ damage secondary to hypertension and in those with multiple cardiovascular risk factors (1). Different risk factor models (e.g. SCORE) that take into consideration the importance of combined risk factors are used to individualise risk assessment and treatment (1). Unfortunately, neither fitness nor the physical activity level are included even in the newer risk factor models.

All of the written guidelines for treatment of hypertension give lifestyle factors, including physical activity, a prominent role, especially in milder and early forms of the disease. Often several months of initial lifestyle modification are recommended (only) in people with BP < 160/90 who show no signs of secondary organ damage or have no other risk factors and are thereby judged to be at low risk for cardiovascular events in the short term.

Increased physical activity together with other lifestyle factors are thus the first treatment in mild hypertension with low cardiovascular risk (1). At blood pressures of 160–179/100–109 mmHg, lifestyle changes, including increased physical activity are initiated for a few weeks before pharmacological treatment is added if needed (1). For all individuals with even higher blood pressure levels, regular physical activity is recommended in addition to medication, as long as the blood pressure is controlled at < 180/105 mmHg, with drug therapy (1). The benefits of combining lifestyle measures and pharmacological antihypertensive treatment should always be stressed.

When there are signs of secondary organ damage, competitive- or elite level sports may be contraindicated (see below).

Prescription

Type of activity

Despite recent studies and an increased interest in the importance of strength training for treating risk factors and hypertension, the main recommendation for primary and secondary prevention in hypertension is still dynamic endurance training, for example, aerobic fitness training, walking, swimming and cycling (1, 21). As a supplement, strength training with low resistance, perhaps 40–50 per cent of maximal capacity (RM = repetition maximum), expressed as “moderate intensity” strength training, and many repetitions could be recommended (19, 34).

Intensity

Most studies show that exercising at 40–70 per cent of VO_2 max (= maximal oxygen uptake; corresponding to 50–85% of maximal individual heart rate) lowers the blood pressure at least as well as more intensive exercise (34). This has also been shown in rat trials, where only animals that exercised at this intensity reached a lower blood pressure than the controls (37). Researchers have even claimed that high intensity exercise training (dynamic > 90% of VO_2 max) such as marathons or competitive running may increase blood pressure. More recent studies appear to confirm the impression that low to medium intensity activity, at a level of only 40 per cent of VO_2 max, is enough to achieve acute post-exercise hypotension (38) and to maintain a more lasting lowering of pressure (14, 39).

What this means in terms of specific activities for a particular individual depends on the individual's fitness level (VO_2 max) prior to the start of exercise training. In the USA, an initial exercise test is often recommended, enabling prescription of a suitable activity according to the outcome of the performance test. This type of testing cannot be recommended as a general practice in Sweden and Norway today for several reasons, among them resources and the fact that it would theoretically result in many unnecessary coronary investigations due to abnormal and false-positive stress tests. In practice, it has been shown that an activity that makes one breathless, but still able to carry on a conversation relatively easily, corresponds to a medium intensity activity (11–13/20 on the Borg RPE scale). For many (untrained) people with hypertension, relatively simple activities, such as walking, are therefore sufficient to achieve a reduction in blood pressure.

Duration

Episodes of physical activity of short duration, such as 3–20 minutes, can reduce blood pressure, but longer durations appear to be connected with greater and more lasting lowering of BP (14, 40). 30- to 45-minute sessions are therefore recommended as suitable for achieving a good pressure-lowering effect (1, 14, 15, 21, 40).

In recent years, there has also been increasing discussion of how physical activity divided into shorter durations may have an equally positive effect as activity of longer duration. A brisk 10-minute walk 4 times per day may be as effective at lowering blood pressure as a 40-minute walk once a day (17).

Accumulated physical activity (walking at 50% of VO_2 max), four 10-minute sessions, even yielded significantly longer lasting post-exercise blood pressure-reduction (11 hours versus 7 hours) than one 40-minute walk, in individuals who had not yet developed hypertension (16).

The total weekly dose of activity also seems to be important. Ishikawa-Takata and colleagues were able to show that 60–90 minutes of activity per week was more effective at lowering pressure than 30–60 minutes per week, over 8 weeks in previously sedentary people with hypertension (41).

Frequency

To take maximum advantage of the acute blood pressure-lowering effect of physical activity, which lasts up to 24 hours, it is usually recommended that exercising be performed on most days of the week. However, five or six days can be just as good as seven due to a lower risk of overuse injuries (34).

The increased physical activity will need to be kept up on a continual basis in order for the blood pressure-reducing effect to be maintained. After 4–6 months, the maximal effect on blood pressure, with respect to pressure-lowering, seems to be attained (15). If the individual stops exercising, the blood pressure returns to the same level as before exercising began (34). This can occur as quickly as within 10 days (17), possibly depending on how long the individual exercised regularly.

Table 2. Recommended exercise training.

Type of training	Prescription
Aerobic fitness training	40–70 per cent of maximal oxygen uptake 5–7 days/week, a minimum of 30 minutes per training session
Strength training	many repetitions and low resistance

Dividing up the activity into 4 sets of 10-minute sessions, for example, can be just as effective as a single 40-minute dose of training per day. Examples of suitable activities (according to ESC classification of sports [42]) may include running, table tennis, cross-country skiing, brisk walking, badminton, orienteering, football, tennis (moderate to high intensity dynamic activity but low static activity). As discussed above, however, the activity best suited for an individual is dependent on that fitness level of that individual.

Mechanisms of blood pressure lowering

The pressure-lowering effect of physical activity is mediated by several mechanisms, either interacting or of different importance in different individuals. However, the blood pressure-lowering effect is independent of a reduction in weight or body fat (34).

Endurance training is associated with decreased vascular resistance involving the sympathetic nervous system and the renin-angiotensin system. Simultaneous cardiovascular risk factors are also positively impacted (21).

Reduced sympathetic activity

Increased sympathetic system activity is believed to play a role in the development of essential hypertension. People with increased noradrenaline levels show a reduction in blood pressure from physical activity parallel to the decrease in noradrenaline levels (21, 43).

Especially, early in the course of hypertension, physical activity plays an important role in reducing blood pressure (34), as the blood pressure increase at this stage is mediated by an increase in cardiac output and secondary, more manifest, vascular changes with increased peripheral resistance has not yet developed. According to Fagard and Cornelissen's meta-analysis (21), physical activity reduces noradrenaline levels by approximately 30 per cent.

Increase in vasodilating agents

It has been proposed that an increase in endorphins as a result of physical activity has a blood pressure-lowering effect post-exercise (44).

Reduced insulin resistance

The link between hypertension and the metabolic syndrome, including obesity, dyslipidemia and increased insulin resistance, has been shown, and has been suggested to play a role in the development of hypertension (5). Physical activity reduces insulin resistance and thereby secondary hyperinsulinemia (45), which is a potential pressure-lowering mediator. Regular physical activity also reduces the risk of developing diabetes (46).

Changes in kidney function

Because the kidneys play a big role in maintaining abnormally high blood pressure, through regulation of sodium and water balance, and thereby cardiac output, some of exercise's positive effects may be mediated by the kidneys (47). For example, plasma-renin is reduced by 20 per cent by aerobic training in hypertensives (21).

Regression of left ventricular hypertrophy

Physical activity leads to a reduction of the left ventricular hypertrophy associated with hypertension to the same degree as pharmacological treatment with diuretics (45). Left ventricular hypertrophy in itself is an independent risk factor for cardiovascular disease and regression produces independent prognostic value (13).

Effects on other risk factors

It is impossible to analyse the effects of physical activity on blood pressure, and thereby reduced mortality/morbidity, in isolation, without taking into consideration the positive effects on other risk factors for cardiovascular disease, such as obesity, hyperinsulinemia and hypertriglyceridemia (21). In addition to the effect on blood pressure alone, the added effects of physical activity reduce overall risk for the patient (1).

Other effects

Known effects of physical activity like improved physical performance (45) lead to a better prognosis in people with hypertension. One controlled study showed that well-trained individuals with hypertension had a lower mortality than untrained individuals with normal blood pressure (48). Physical activity also reduces inflammatory parameters such as hs-CRP, which is a risk marker for cardiovascular disease. Also hs-CRP is inversely related to level of fitness in people with hypertension (49). Physical activity is associated with improved quality of life in addition to blood pressure reduction in these patients (50). A new study that compares different treatment regimens shows physical activity to be most strongly associated with improved quality of life in several dimensions, most markedly in older women (51).

Interactions

Beta blockers

Treatment with beta blockers leads to a lowering of the maximal heart rate by about 30 beats per minute (15). In addition to lowering resting blood pressure, beta blockers reduce the activity-induced elevation of systolic blood pressure. In comparison with other antihypertensive drugs, the rate pressure product (heart rate multiplied by blood pressure) increases less at a given level of physical intensity with beta blocker therapy (52). This yields a reduction of the patient's maximal performance capacity (15), but is also a positive effect, especially in people with abnormally large increases in blood pressure during dynamic exercise. For normal, medium intensity activity, this likely plays a minor role. But a person with higher demands on performance, for example, a more fit, active runner, may find it hard to accept beta blocker therapy.

Whether or not beta blockade reduces resting energy expenditure and/or reduce weight loss from physical activity (53) has been discussed. However, it is possible that beta blockade mitigates the increase in the energy expenditure observed in physical activity (54).

Diuretics

Has potentially negative effects through increasing the risk for dehydration in warm weather, as well as increasing the risk for hypokalaemia (15).

ACE inhibitors

ACE inhibitors are a first choice for physically active people with hypertension. They can help to lower blood pressure after activity, which can create problems in dehydrated patients, for example, patients with diarrhoea, especially in warmer climates.

Angiotensin receptor blockers

Another possible first choice. At present, there is limited experience and the same precaution must be taken as with ACE inhibitors. They have been shown to reduce blood pressure response in connection with physical exercise (55).

Calcium channel blockers

A possible drug of first choice. There is a risk for a drop in blood pressure immediately after exercise due to vasodilatation (widening of the blood vessels).

Alpha blockers

Alpha blockers are a good secondary alternative, with minor impact on maximal performance capacity (56, 57).

Contraindications

A systolic blood pressure over 200 mmHg or a diastolic pressure over 115 mmHg should contraindicate physical activity until the pressure has stabilised below these levels with blood pressure-lowering medication (15). The American College of Sports Medicines (ACSM) guidelines recommend that individuals with blood pressure > 180/105 first begin pharmacological treatment before any regular physical activity is resumed or started (relative contraindication) (34).

ACSM also recommends, however, that caution be taken with very intensive dynamic training (90–100% of VO_2 max) such as extreme elite sports in people with hypertension, as well as heavier strength training (weight lifting etc.) (34). In the case of strenuous

strength training, extremely high blood pressure can be measured in the heart's left ventricle (> 300 mmHg), which is potentially dangerous. ACSM recommends some caution in the case of established hypertrophy of the left ventricle, which means that these individuals should possibly exercise in the lower region of the proposed interval (40–70% of VO_2 max) (34).

Side-effects

Increase in blood pressure

When the intensity of dynamic or static training is too high, the result can instead be elevated blood pressure (see above).

Stroke

Side-effects can also arise due to the high blood pressure that can develop in people with hypertension exercising at too high an intensity. Research has, however, not been able to show an increased incidence of stroke in these people, and not from strength training either.

General side-effects

Joint injuries from overloading (often concurrent obesity and hypertension) may develop.

Dehydration, electrolyte disorders, hypotension

These side-effects can arise to varying degrees, due in part to the physical activity and in part to possible medications.

Sudden death

A very small increased risk for sudden cardiac death *during* physical activity is offset by a significantly greater decrease in the long-term morbidity/mortality risk.

References

1. ESC. 2007 guidelines for the management of arterial hypertension. *J Hypertension* 2007;25:1105-87.
2. WHO. The World Health Report. Reducing risks, promoting healthy life. Geneva: World Health Organization; 2002.
3. Hajjar I, Kotchen T. Trends in prevalence, awareness, treatment and control of hypertension in the United States, 1998–2000. *JAMA* 2003;290:199-206.
4. Kearney PM, Whelton P, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension. Analysis of worldwide data. *Lancet* 2005;365:217-23.
5. Dahlöf B. Hypertonihandboken [The Hypertension Handbook]. Sollentuna: Merck, Sharp & Dohme (Sweden) AB; 2000.
6. Geleijnse JM, Kok FJ, Grobbee DE. Impact of dietary and lifestyle factors on the prevalence of hypertension in Western populations. *Eur J Public Health* 2004;14:235-9.
7. Vasan RS, Larson MG, Leip EP, Evans JC, O'Donnell CJ, Kannel WB, et al. Impact of high-normal blood pressure on the risk of cardiovascular disease. *N Engl J Med* 2001;345:1291-7.
8. Lewington S, Clarke R, Qizilbach N, Peto R, Collins R, Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality. A meta-analysis of individual data from one million adults in 61 prospective studies. *Lancet* 2002;360:1903-13.
9. Börjesson M, Dahlöf B. Fysisk aktivitet har en nyckelroll i hypertonibehandlingen [Physical activity has a key role in hypertension therapy]. *Läkartidningen* 2005;102:123-9.
10. Wolf-Meier K, Cooper RS, Kramer H, Banegas JR, Giampaoli S, Joffres MR. Hypertension treatment and control in five European countries, Canada, and the United States. *Hypertension* 2004;43:10-7.
11. Evenson KR, Stevens J, Thomas R, Cai J. Effect of cardiorespiratory fitness on mortality among hypertensive and normotensive women and men. *Epidemiology* 2004;15:565-72.
12. Sandvik L, Erikssen J, Thaulow E, Erikssen G, Mundal R, Rodahl K. Physical fitness as a predictor of mortality in healthy middle-aged men. *N Engl J Med* 1993;328:533-7.
13. Devereaux RB, Wachtell K, Gerds E, Boman K, Nieminen MS, Papademitrou V. Prognostic significance of left ventricular mass change during treatment of hypertension. *JAMA* 2004;292:2350-6.
14. Guidry MA, Blanchard BE, Thompson PD, Maresh CM, Seip RL, Taylor AL, et al. The influence of short and long duration on the blood pressure response to an acute bout of dynamic exercise. *Am Heart J* 2006;151:1322.e5-12.
15. Gordon NF. Hypertension. In: Durstine JL, Ed. ACSM's exercise management for persons with chronic diseases and disabilities. Champaign (IL): Human Kinetics; 1997.
16. Park S, Rink LD, Wallace JP. Accumulation of physical activity leads to greater blood pressure reduction than a single continuous session, in prehypertension. *J Hypertens* 2006;24:1761-70.

17. Elley R, Bagrie E, Arroll B. Do snacks of exercise lower blood pressure? A randomised crossover trial. *NZMJ* 2006;119:1-9.
18. Tipton CM. Exercise and hypertension. In: Shephard RJ, Miller HSJ, Eds. *Exercise and the heart in health and disease*. 2. edn. New York: Marcel Dekker, Inc.; 1999, pp. 463-88.
19. Cornelissen VA, Fagard RH. Effect of resistance training on resting blood pressure. A meta-analysis of randomized controlled trials. *J Hypertens* 2005;23:251-9.
20. Cheung BMY, Lo JLF, Fong DYJ, Chan MY, Wong SHT, Wong VCW, et al. Randomised controlled trial of qigong in the treatment of mild essential hypertension. *J Hum Hypertension* 2005;19:697-704.
21. Fagard RH, Cornelissen VA. Effect of exercise on blood pressure control in hypertensive patients. *Eur J Cardiovasc Prev Rehabil* 2007;14:12-7.
22. Ketelhut RG, Franz IW, Scholze J. Regular exercise as an effective approach in anti-hypertensive therapy. *Med Sci Sports Exerc* 2004;36:4-8.
23. Santaella DF, Ara jo EA, Ortega KC, Tinucci T, Mion DJ, Negrao CE, et al. Aftereffects of exercise and relaxation on blood pressure. *Clin J Sport Med* 2006;16:341-7.
24. Svetkey LP, Erlinger TP, Vollmer WM, Feldstein A, Cooper LS, Appel LJ, et al. Effect of lifestyle modifications on blood pressure by race, sex, hypertension status, and age. *J Hum Hypertension* 2005;19:21-31.
25. Stewart KJ, Bacher AC, Turner KL, Fleg JL, Hees PS, Shapiro EP, et al. Effect of exercise on blood pressure in older patients. *Arch Intern Med* 2005;165:756-62.
26. Lee L-L, Arthur A, Avis M. Evaluating a community-based walking intervention for hypertensive older people in Taiwan. A randomized controlled trial. *Prev Med* 2006;44:160-6.
27. Paffenbarger RS Jr, Jung DL, Leung RW, Hyde RT. Physical activity and hypertension. An epidemiological view. *Ann Med* 1991;23:319-27.
28. Barengo NC, Hu G, Kastarinen M, Lakka TA, Pekkarinen H, Nissanen A, et al. Low physical activity as a predictor for antihypertensive drug treatment in 25–64 year-old population in Eastern and South-Western Finland. *J Hypertens* 2005;23:293-9.
29. Stamler R, Stamler J, Gosch FC, Civinelli J, Fishman J, McKeever P, et al. Primary prevention of hypertension by nutritional-hygienic means. *JAMA* 1989;262:1801-7.
30. Greenfield JR, Samaras K, Campbell LV, Jenkins AB, Kelly PJ, Spector TD, et al. Physical activity reduces genetic susceptibility to increased central systolic pressure augmentation. A study of female twins. *J Am Coll Cardiol* 2003;42:264-70.
31. Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA. American College of Sports Medicine. Position stand. Exercise and hypertension. *Med Sci Sports Exerc* 2004;36:533-53.
32. Wilson MF, Sung BH, Pincomb GA, Lovallo WR. Exaggerated pressure response to exercise in men at risk for systemic hypertension. *Am J Cardiol* 1990;66:731-6.
33. Benbassat J, Fromm PF. Blood pressure response to exercise as a predictor of hypertension. *Arch Intern Med* 1986;146:2053-5.

34. American College of Sports Medicine. Position stand. Physical activity, physical fitness, and hypertension. *Med Sci Sports Exerc* 1993;25:i-x.
35. Laukkanen JA, Kurl S, Salonen R, Lakka TA, Rauramaa R, Salonen JT. Systolic blood pressure during recovery from exercise and the risk of acute myocardial infarction in middle-aged men. *Hypertension* 2004;44:820-5.
36. Erikssen G, Bodegard J, Bjornholt JV, Liestol K, Thelle DS, Erikssen J. Exercise testing of healthy men in a new perspective. From diagnosis to prognosis. *Eur Heart J* 2004;25:978-86.
37. Tipton CM, MacMahon S, Leininger JR, Pauli EL, Lauber C. Exercise training and incidence of cerebrovascular lesions in stroke-prone spontaneously hypertensive rats. *J Appl Physiol* 1990;68:1080-5.
38. Smelker CL, Foster C, Maher MA, Martinez R, Porcari JP. Effect of exercise intensity on postexercise hypotension. *J Cardiopulm Rehabil* 2004;24:269-73.
39. Pescatello LS, Guiridy MA, Blanchard BE, Kerr A, Taylor AR, Johnson AN, et al. Exercise intensity alters postexercise hypotension. *J Hypertens* 2004;22:1881-8.
40. Mach C, Foster C, Brice G, Mikat RP, Porcari JP. Effect of exercise duration on post-exercise hypotension. *J Cardiopulm Rehabil* 2005;25:366-9.
41. Ishikawa-Takata K, Ohta T, Tanaka H. How much exercise is required to reduce blood pressure in essential hypertensives. A dose-response study. *Am J Hypertens* 2003;16:629-33.
42. Pelliccia A, Fagard R, Bjornstad HH, Anastassakis A, Arbustini E, Assanelli D, et al. Recommendations for competitive sports participation in athletes with cardiovascular disease. ESC Report. *Eur Heart J* 2005;26:1422-45.
43. Duncan JJ, Farr JE, Upton J, Hagan RD, Oglesby ME, Blair SN. The effects of aerobic exercise on plasma catecholamines and blood pressure in patients with mild hypertension. *JAMA* 1985;254:2609-13.
44. Thorén P, Floras JS, Hoffman P, Seals DR. Endorphins and exercise. Physiological mechanisms approach. *Med Sci Sports Exerc* 1990;22:17-28.
45. Rinder MR, Spina RJ, Peterson LR, Koenig CJ, Florence CR, Ehsani AA. Comparison of effects of exercise and diuretic on left ventricular geometry, mass, and insulin resistance in older hypertensive adults. *Am J Physiol Regul Integr Comp Physiol* 2004;287:R360-8.
46. Fossum E, Gleim GW, Kjeldsen SE, Kizer JR, Julius S, Devereaux RB, et al. The effect of baseline physical activity on cardiovascular outcomes and new-onset diabetes in patients treated for hypertension and left ventricular hypertrophy. The LIFE study. *J Intern Med* 2007;262:439-48.
47. Kenney WL, Zambraski EJ. Physical activity in human hypertension. A mechanisms approach. *Sports Med* 1984;1:459-73.
48. Blair SN, Kohl HWI, Paffenbarger Jr RS, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. *JAMA* 1989;262:2395-401.

49. Hjelstuen A, Anderssen SA, Holme I, Seljeflot I, Klemsdal TO. Markers of inflammation are inversely related to physical activity and fitness in sedentary men with treated hypertension. *Am J Hypertens* 2006;19:669-75.
50. Tsai J-C, Yang H-Y, Wang W-H, Hsieh M-H, Chen P-T, Kao C-C, et al. The beneficial effect of regular endurance exercise training on blood pressure and quality of life in patients with hypertension. *Clin Exp Hypert* 2004;26:255-65.
51. Fernandez FJC, Garcia MTM, Alvarez CR, Giron MJI, Aguirre-Jaime A. Is there an association between physical exercise and the quality of life of hypertensive patients? *Scand J Med Sci Sports* 2007;17:348-55.
52. Kokkinos P, Chrysohoou C, Panagiotakos D, Narayan P, Greenberg M, Singh S. Beta-blockade mitigates exercise blood pressure in hypertensive male patients. *J Am Coll Cardiol* 2006;47:794-8.
53. Gondoni LA, Tagliaferri MA, Titon AM, Nibbio F, Liuzzi A, Leonetti G. Effect of chronic treatment with beta-blockers on resting energy expenditure in obese hypertensive patients during a low-calorie and physical training program. *Nutr Metab Cardiovasc Dis* 2003;13:232-7.
54. Bélanger M, Boulay P. Effect of an aerobic exercise training program on resting metabolic rate in chronically beta-adrenergic blocked hypertensive patients. *J Cardiopulm Rehabil* 2005;25:354-60.
55. Nashar K, Nguyen JP, Jesri A, Morrow JD, Egan BM. Angiotensin receptor blockade improves arterial distensibility and reduces exercise-induced pressor responses in obese hypertensive patients with the metabolic syndrome. *Am J Hypertens* 2004;17:477-82.
56. Fahrenbach MC, Yurgalevitch SM, Zmuda JM, Thompson PD. Effect of doxazosin or atenolol on exercise performance in physically active, hypertensive men. *Am J Cardiol* 1995;75:258-63.
57. Tomten SE, Kjeldsen SE, Nilsson S, Westheim AS. Effect of alpha-1 adrenoceptor blockade on maximal VO_2 and endurance capacity in well trained athletic hypertensive men. *Am J Hypertens* 1994;7:603-8.