Managing Hypertension in Athletes and Physically Active Patients

MARK W. NIEDFELDT, M.D., Medical College of Wisconsin, Milwaukee, Wisconsin

Athletes and other physically active patients should be screened for hypertension and given appropriate therapy if needed. Mild hypertension should be treated with nonpharmacologic measures for six months. If blood pressure control is adequate, lifestyle modifications are continued. If control is inadequate, low-dose therapy with an angiotensin-converting enzyme inhibitor or a calcium channel blocker may be started. A thiazide diuretic may be used as first-line treatment for hypertension in casually active patients; however, diuretic therapy is less desirable in high-intensity or endurance athletes because of the risk of hypovolemia or hypokalemia. If beta blockade is needed, a combined alpha-beta blocker may be the best choice. When the target blood pressure is achieved, long-term follow-up care and management should be emphasized. If excellent control is maintained for six to 12 months, medication may be reduced or withdrawn in a small number of patients. If the target blood pressure is not achieved, the medication dosage may be adjusted, or a second medication, usually a diuretic, may be added. Physicians need to be aware of the effects of various medications on exercise tolerance and the rules for participation established by sports regulatory bodies (Am Fam Physician 2002;66:445-52,457-8. Copyright© 2002 American Academy of Family Physicians.)

A patient information handout on high blood pressure and exercise, written by the author of this article, is provided on page 457.

Members of various family practice departments develop articles for "Practical Therapeutics." This article is one in a series coordinated by the Department of Family and Community Medicine at the Medical College of Wisconsin, Milwaukee. Guest editors of the series are Linda N. Meurer, M.D., M.P.H., and Douglas Bower, M.D.

Athletes and other physically active patients are usually thought to be free of cardiovascular disease and hypertension because of their apparently high level of fitness. Indeed, the overall prevalence of high blood pressure in these groups is approximately 50 percent lower than in the general population.[1] However, the risk of hypertension is increased in some athletes and physically active patients, including blacks, the elderly, persons who are obese, and those with diabetes, renal disease, or a family history of hypertension. Wheelchair athletes with spinal cord injuries may also have hypertension because of loss of autonomic control of blood pressure.[2]

Hypertension often begins in early adulthood. It becomes more prevalent with increasing age, affecting 5 to 10 percent of adults 20 to 30 years of age and 20 to 25 percent of adults 30 to 60 years of age.[3] Almost 80 percent of adolescents found to have a blood pressure above 142/92 mm Hg during a presports-participation physical examination eventually develop chronically elevated blood pressure.[4]

The risk of hypertension is increased in some athletes and physically active patients, including blacks, the elderly, persons who are obese, and those with diabetes, renal disease, or a family history of hypertension.

All athletes and physically active patients should be screened for hypertension. If the condition is diagnosed, appropriate treatment should be started to reduce the risk of morbidity and mortality associated with cardiovascular disease.[5]

Hypertension Classification and Secondary Hypertension

The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure emphasizes the progressive nature of hypertension and divides blood pressure into six classes *(Table 1)*.[5] Most athletes and physically active patients with hypertension fall into stage 1 or 2.

Secondary hypertension develops in fewer than 5 percent of athletes and physically active patients.[6] It tends to occur in younger patients, adult patients with rapid onset of severe hypertension, and patients with hyper-

TABLE 1
Classification of Blood Pressure*

Class	*Systolic blood pressure (mm Hg)*	*Diastolic blood pressure (mm Hg)*
Optimal	<120	<80
Normal	<130	<85
High normal	130 to 139	85 to 89
Hypertension		
Stage 1	140 to 159	90 to 99
Stage 2	160 to 179	100 to 109
Stage 3	≥180	≥110

**—If the systolic blood pressure and the diastolic blood pressure fall into different classes, the higher class should be used.*

Adapted with permission from The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413-46.

tension that responds poorly to routine therapies. The most common cause of secondary hypertension is vascular or parenchymal renal disease.[6]

Hypertension can also occur secondary to estrogen in oral contraceptive pills, which are commonly taken by female athletes. This secondary hypertension generally develops soon after they start taking the pills. About 5 percent of all women who take oral contraceptive pills develop hypertension over a five-year period.[7]

The Author

MARK W. NIEDFELDT, M.D., is assistant professor of family and community medicine and orthopedic surgery and associate director of the sports medicine fellowship program at the Medical College of Wisconsin, Milwaukee. Dr. Niedfeldt graduated from the Medical College of Wisconsin, where he also completed a family practice residency and sports medicine fellowship.

Address correspondence to Mark W. Niedfeldt, M.D., Departments of Family and Community Medicine and Orthopaedic Surgery, Medical College of Wisconsin, 2320 N. Lake Dr., Milwaukee, WI 53211 (e-mail: mniedfel@mcw.edu). Reprints are not available from the author.

Clinical Evaluation

In athletes and other physically active patients with hypertension, the history should focus on behaviors that may affect blood pressure, such as a high intake of sodium and saturated fats (e.g., in processed and "fast" foods) and the use of alcohol, drugs (specifically, stimulants taken before competitions, or cocaine), tobacco, or anabolic steroids *(Table 2)*.[5,7-9] Many over-the-counter medications, including nonsteroidal anti-inflammatory drugs (NSAIDs), caffeine, diet pills, and decongestants, can also cause blood pressure to rise.

Patients should also be questioned about the use of herbs and dietary supplements, with special attention given to substances purported to increase energy or control weight. These supplements often contain "natural" substances such as guanara, ma huang, and ephedra, which are stimulants.

Stress levels should be evaluated. Chronic environmental or social stress may result in higher levels of circulating catecholamines and chronic neurogenic activation of the sympathetic nervous system, which can contribute to hypertension.[8]

The clinical evaluation should include proper measurement of blood pressure[7] and laboratory tests directed at excluding causes of secondary hypertension or identifying end-organ damage. Studies should include an electrocardiogram, a complete blood count, urinalysis, and measurements of sodium, potassium, blood urea nitrogen, creatinine, fasting glucose, and total, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) cholesterol levels. Other studies and further evaluation may be performed if a secondary cause of hypertension is suspected.

Treatment

NONPHARMACOLOGIC THERAPY

Compared with the general population, athletes and other physically active patients are often more motivated to comply with nonpharmacologic interventions, because

TABLE 2
Risk Factors for Hypertension in Athletes and Other Physically Active Patients

High sodium intake
Excessive alcohol consumption (binge drinking)
Illicit drug use (e.g., cocaine)
Anabolic steroid use
Stimulant use (e.g., in supplements taken to enhance energy or control weight)
High stress levels
Male gender
Race (blacks affected more often than whites by about a 2-to-1 ratio, and Asians affected the least)
Family history of hypertension or cardiac disease in men over 55 years of age and women over 65 years of age
Diabetes mellitus or glucose intolerance
Smoking or chewing tobacco
Obesity

Information from references 5, 7, 8, and 9.

these measures have virtually no side effects. Although lifestyle modifications cannot eliminate the need for antihypertensive drug therapy in all patients, dietary and behavioral changes may reduce the amount of medication needed and, thus, the possibility of side effects. Dietary and lifestyle changes may include decreasing sodium intake, increasing potassium intake, losing weight, decreasing alcohol consumption, avoiding stimulant use, applying relaxation techniques, and performing aerobic exercise.

Dietary Changes. A reduction in sodium intake can lead to a decrease in blood pressure.[5] In particular, patients should be advised to reduce their intake of processed foods such as luncheon meat and fast foods. Processed foods provide 75 percent of the sodium recommended for the typical American diet.[9] These foods are particularly common in the diets of adolescent athletes. Blacks, older persons, and those with diabetes mellitus seem to be especially sensitive to the effects of dietary sodium.[9]

High dietary potassium intake may improve blood pressure control, especially in endurance athletes, who may tend to be hypokalemic.

Potatoes and bananas, as well as many other fruits, contain significant amounts of potassium. These foods should be included in the diet of athletes and other physically active patients. High dietary potassium intake may provide some protection against high blood pressure or may improve blood pressure control.[10] A high-potassium diet is especially important in endurance athletes, who may tend to be hypokalemic.[5]

Calcium or magnesium supplementation for the sole purpose of improving blood pressure control is not routinely recommended in physically active patients.[5]

Weight Loss. Losing just 4.5 kg (10 lb) can reduce blood pressure in overweight patients who have hypertension.[11] Loss of this much weight also seems to enhance the blood pressure–lowering effects of many medications.[12] The weight reduction plan should include foods that are high in fiber and low in saturated fats.[13]

Lifestyle Changes. Excessive alcohol use can decrease the effectiveness of antihypertensive drug therapy. Adults should limit alcohol intake to the equivalent of two beers per day. Women and lighter weight persons should consume no more than the equivalent of one beer per day.[5]

Some athletes routinely use biofeedback, muscle relaxation techniques, meditation, yoga, and stress management techniques. These stress reduction tools may have value as adjunctive therapy in patients with hypertension.

Regular aerobic exercise adequate to achieve moderate fitness can lower blood pressure, enhance weight loss, and reduce mortality.[14] The effects of exercise on hypertension are

even more dramatic in patients with hypertension secondary to renal dysfunction.

Recommendations on exercise and sports participation for patients with hypertension are provided in *Table 3*.[15]

PHARMACOLOGIC THERAPY

Athletes and other physically active patients need to monitor medication effects, because some antihypertensive drugs may have an adverse influence on exercise tolerance. Other drugs, including NSAIDs, may decrease the action of antihypertensive medications, including diuretics, beta blockers, and angiotensin-converting enzyme (ACE) inhibitors.[16] Physicians and patients also need to be aware that the U.S. Olympic Committee (USOC) and the National Collegiate Athletic Association (NCAA) have banned the use of some antihypertensive medications.[16-18] The effects of antihypertensive drug classes are summarized in *Table 4*.[5,6,16-21]

Diuretics. Both thiazide and loop diuretics decrease plasma volume, cardiac output, and vascular resistance.[20] The thiazide diuretics have less pronounced effects.

Thiazide diuretics are often recommended as initial therapy in patients with hypertension. In several randomized, controlled trials (conducted primarily in the elderly),[22-28] these agents have been associated with decreases in both mortality and morbidity.

Thiazide diuretics are useful as second-line therapy in salt-sensitive athletes and physically active patients with hypertension.[5] These agents should be given in a low dosage and, in some patients, combined with a potassium-sparing agent. Thiazide diuretics are inexpensive and a good choice in patients who exercise only casually, in physically active elderly patients, and in black patients. Possible side effects include hypovolemia, orthostatic hypotension, and urinary loss of potassium and magnesium. These side effects can lead to muscle cramps, arrhythmias, and rhabdomyolysis in patients who are exercising intensely or competing in warm weather.

The side effects associated with thiazide diuretics are magnified with the more potent loop diuretics. Consequently, loop diuretics are inappropriate for use in the treatment of hypertension in athletes and other physically active patients. These agents have also been shown to cause short-term increases in plasma cholesterol, glucose, and uric acid levels.[21]

Sports regulatory bodies have banned the use of all diuretics. These agents cannot be used by elite athletes who are required to undergo drug testing.[16-18]

ACE Inhibitors. These agents block the conversion of angiotensin I to angiotensin II, which is a potent vasoconstrictor and a source

TABLE 3
Exercise and Sports Participation in Athletes and Other Physically Active Persons with Hypertension

Exercise

The recommended mode, frequency, duration, and intensity of exercise are generally the same as those for persons without hypertension.

Sports participation

Blood pressure should be controlled before resumption of participation in vigorous sports, because both dynamic and isometric exercise can cause remarkable increases in blood pressure.

Recommendations on exercise restrictions

High-normal blood pressure	No restrictions
Controlled mild to moderate hypertension (<140/90 mm Hg)	No restrictions on dynamic exercise; possible limit on isometric training or sports in some patients
Uncontrolled hypertension (>140/90 mm Hg)	Limited to low-intensity dynamic exercise; avoid isometric sports.
Controlled hypertension with end-organ damage	Limited to low-intensity dynamic exercise; avoid isometric sports.
Severe hypertension with no end-organ involvement	Limited to low-intensity dynamic exercise, with participation only if blood pressure is under adequate control.
Secondary hypertension of renal origin	Limited to low-intensity dynamic exercise; avoid "collision" sports that could lead to kidney damage.

Information from 26th Bethesda Conference: recommendations for determining eligibility for competition in athletes with cardiovascular abnormalities. January 6-7, 1994. J Am Coll Cardiol 1994;24:845-99.

of sodium retention.[19] ACE inhibitors are associated with a slight decrease in heart rate, an increase in stroke volume, and a decrease in total peripheral resistance.[20]

ACE inhibitors have been shown to have beneficial effects in patients with heart failure, systolic dysfunction or nephropathy. They reverse ventricular hypertrophy and microalbuminuria, with preservation of renal function. In exercise, ACE inhibitors have no major effects on energy metabolism and cause no impairment of maximum oxygen uptake. In general, these drugs have no deleterious effects on training or competition.[20]

The major side effect of ACE inhibitors is a dry, nonproductive cough. Because there have been anecdotal reports of postural hypotension after intense exercise in patients taking ACE inhibitors, an adequate cool-down period is recommended.

ACE inhibitors are excellent for treating mild to moderate hypertension. They are often the first-line agents for the treatment of high blood pressure in physically active patients, especially those with diabetes.[5] Their effectiveness may be improved by adding a thiazide in a low dosage, with the drugs taken separately or in combination.

The potassium-sparing effect of ACE inhibitors may be increased when these agents are taken concomitantly with NSAIDs.[19] Use of ACE inhibitors is contraindicated in pregnancy. Therefore, patients of childbearing age should use some form of contraception if they are taking an ACE inhibitor.

Angiotensin-II receptor blockers produce similar effects as ACE inhibitors. However, because of their action at the receptor level, they do not cause a dry cough. Currently, insufficient data are available to document whether angiotensin-II receptor blockers have cardiac and renal protective effects. Therefore, these agents are generally recommended only for patients who cannot tolerate ACE inhibitors.[5]

Alpha Blockers. The $alpha_1$-receptor antagonists competitively block postsynaptic $alpha_1$ arteriolar smooth muscle receptors. They decrease systemic vascular resistance, with no reflex increase in heart rate or cardiac output. A first-dose hypotensive effect can occur, especially in the elderly.

Athletes who take beta blockers perceive greater exertion during exercise, which may affect adherence to the prescribed medication regimen.

Alpha blockers cause no major changes in energy metabolism during exercise, and maximum oxygen uptake is preserved. Therefore, these agents have no major effects on training or sports performance.[20] Alpha blockers have been used in athletes with diabetes mellitus who have hypertension and hypercholesterolemia, because they do not exacerbate these conditions.[7]

The doxazosin arm of the ongoing Antihypertensives and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)[29] was discontinued because of an increased incidence of congestive heart failure, compared with use of a diuretic. The ALLHAT findings should be taken into consideration, especially in athletes older than 55 years.

Centrally acting alpha agonists have no major effects on training or sports performance.[19] Because of their side effects, however, these agents are rarely used. These effects may include mild to moderate drowsiness, dry mouth, and impotence. Rebound hypertension can occur with the abrupt discontinuation of orally administered clonidine (Catapres).[7]

Beta Blockers. Noncardioselective beta blockers significantly decrease contractility of the heart and decrease heart rate. Systemic vascular resistance is increased, especially in the muscle and skin. Because these drugs inhibit lipolysis and glycogenolysis, hypoglycemia may occur after intense exercise. In addition, athletes who take beta blockers perceive greater exertion during exercise, which may affect adherence to the prescribed medication regimen.[20] An increased total choles-

TABLE 4
Summary of Pharmacologic Treatment for Hypertension in Athletes and Other Physically Active Patients

Drug class	*Heart rate*	*Stroke volume*	*Cardiac output*	*Vascular resistance*	*Plasma volume*	*Effects on training*
Thiazide diuretics*	No effect	Decrease	Decrease	Decrease	Significant decrease	No effect or decrease in endurance
ACE inhibitors†	Slight increase	Increase	Increase	Decrease	No effect	No effect
Alpha blockers	No effect	No effect	No effect	Decrease	No effect	No effect
Beta blockers	Significant decrease	No effect	Significant decrease	Increase	No effect	Significant decrease
Calcium channel blockers	Decrease, increase, or no effect	No effect or decrease	No effect or decrease	Decrease	No effect or increase	No effect

CHF = congestive heart failure; USOC = U.S. Olympic Committee; NCAA = National Collegiate Athletic Association; ACE = angiotensin-converting enzyme; BPH = benign prostatic hyperplasia.

**—Loop diuretics are inappropriate for the treatment of hypertension in competitive athletes and other physically active patients.*

terol level and a decreased HDL cholesterol level may also be noted.[7]

Although cardioselective beta blockers have fewer side effects than noncardioselective agents, they also impair cardiac output and maximum oxygen uptake, particularly in athletes. Cardioselective beta blockers should not be used in athletes and other physically active patients unless there is an underlying condition (e.g., coronary artery disease) that requires their use.[20]

When combined alpha-beta blockers are used, the beta effects are greater than the alpha effects. There is a decrease in the systemic vascular resistance, but less impairment of muscle blood flow and maximum oxygen uptake. If beta blockade is necessary, a combined alpha-beta blocker may be the best choice.[21]

The USOC has banned the use of beta blockers in athletes participating in precision events such as archery, shooting, diving, and ice skating.[16-18]

Calcium Channel Blockers. These drugs inhibit calcium slow-channel conduction, thereby reducing the calcium concentration in vascular smooth muscle cells, which results in decreased systemic vascular resistance with generalized vasodilation.[19] Calcium channel

Side effects	*Patients in whom drug class is recommended*	*Patients in whom drug class should be avoided*	*Banned status*
Hypovolemia, orthostatic hypotension, and urinary loss of potassium and magnesium, which can lead to muscle cramps, arrhythmias, and rhabdomyolysis in patients exercising intensely or competing in warm weather	Elderly patients, black patients, patients with CHF	Endurance athletes, collegiate athletes	Use banned by USOC and NCAA
Dry, nonproductive cough (angiotensin I blockers)	Patients with diabetes mellitus, renal insufficiency, CHF, asthma, or hyperlipidemia	Female patients who are not using contraception	None
First-dose hypotensive effect with alpha$_1$ blockers, especially in elderly patients Centrally acting agents may cause drowsiness, dry mouth, and impotence; rebound hypertension can occur with abrupt discontinuation of clonidine (Catapres).	Patients with hyperlipidemia or BPH	May want to avoid in men older than 55 years	None
Increase in perceived exertion levels, impairment of cardiac output and maximum oxygen uptake, earlier fatigue and lactate threshold, possible exacerbation of exercise-induced bronchospasm or asthma	Patients with coronary artery disease	Patients with asthma, endurance athletes, collegiate athletes	Use banned in precision sports (i.e., shooting, archery, diving, ice skating)
Nondihydropyridines (e.g., verapamil [Calan], diltiazem [Cardizem]) can cause heart rate suppression and minor impairment of maximum heart rate, decreased left ventricular contractility, and constipation. Dihyrdopyridines (e.g., amlodipine [Norvasc], nifedipine [Procardia]) can cause reflex tachycardia, fluid retention, and vascular headaches.	Patients with asthma, black patients	None	None

†—Because of insufficient data documenting cardiac and renal protective effects, angiotensin-II receptor blockers are generally recommended only in patients who cannot tolerate ACE inhibitors. Angiotensin-II receptor blockers do not cause dry, nonproductive cough.

Information from references 5, 6, and 16 through 21.

blockers are effective in reversing ventricular hypertrophy.

Dihydropyridines such as amlodipine (Norvasc) and nifedipine (Procardia) can cause reflex tachycardia, fluid retention (pedal edema), and vascular headaches. Nondihydropyridines such as verapamil (Calan) and diltiazem (Cardizem) can cause heart rate suppression, minor impairment of maximal heart rate, decreased left ventricular contractility, and constipation.[5]

Calcium channel blockers have no major effects on energy metabolism during exercise, and maximum oxygen uptake is generally preserved.[20] There is a potential for competitive "steal" of muscle blood flow (because of vasodilatation) and earlier onset of the lactate threshold.[30] However, calcium channel blockers, especially the dihydropyridines, are generally well tolerated and effective in physically active patients. They are often used as first-line agents in black athletes.[5]

The author thanks Larry Duenk, M.D., Department of Family and Community Medicine, Medical College of Wisconsin, Milwaukee, for reviewing the manuscript.

The author indicates that he does not have any conflicts of interest. Sources of funding: none reported.

REFERENCES

1. Lehmann M, Durr H, Merkelbach H, Schmid A. Hypertension and sports activities: institutional experience. Clin Cardiol 1990;13:197-208.
2. Swain R, Kaplan B. Treating hypertension in active patients: which agents work best with exercise? Phys Sportsmed 1997;25:47-64.
3. Gifford RW Jr., Kirkendall W, O'Connor DT, Weidman W. Office evaluation of hypertension. A statement for health professionals by a writing group of the Council for High Blood Pressure Research, American Heart Association. Circulation 1989;79:721-31.
4. Tanji JL. Tracking of elevated blood pressure values in adolescent athletes at 1-year follow-up. Am J Dis Child 1991;145:665-7.
5. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413-46.
6. Hanson P, Andrea BE. Treatment of hypertension in athletes. In: DeLee J, Drez D, Stanitski CL, eds. Orthopaedic sports medicine: principles and practice. Philadelphia: Saunders, 1994:307-19.
7. Kaplan NM, Lieberman E. Clinical hypertension. 6th ed. Baltimore: Williams & Wilkins, 1994:23-46,343-66,191-281.
8. Julius S, Nesbitt S. Sympathetic overactivity in hypertension. A moving target. Am J Hypertens 1996;9:S113-20.
9. Weinberger MH. Salt sensitivity of blood pressure in humans. Hypertension 1996;27(3 pt 2):481-90.
10. Whelton PK, He J, Cutler JA, Brancati FL, Appel LJ, Follmann D, et al. Effects of oral potassium on blood pressure. Meta-analysis of randomized controlled clinical trials. JAMA 1997;277:1624-32.
11. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. The Trials of Hypertension Prevention, phase II. The Trials of Hypertension Prevention Collaborative Research Group. Arch Intern Med 1997;157:657-67.
12. Neaton JD, Grimm RH Jr, Prineas RJ, Stamler J, Grandits GA, Elmer PJ, et al. Treatment of Mild Hypertension Study. Final results. Treatment of Mild Hypertension Study Research Group. JAMA 1993;270:713-24.
13. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med 1997;336:1117-24.
14. Petrella RJ. How effective is exercise training for the treatment of hypertension? Clin J Sport Med 1998;8:224-31.
15. 26th Bethesda Conference: recommendations for determining eligibility for competition in athletes with cardiovascular abnormalities. January 6-7, 1994. J Am Coll Cardiol 1994;24:845-99.
16. Fuentes RJ, Rosenberg JM. Athletic drug reference '99: complies with NCAA and USOC rules. Durham, N.C.: Glaxco Wellcome; Clean Data, 1999:28-36,52-4,317-408.
17. IOC prohibited classes of substances and prohibited methods of doping. Retrieved October 2001, from http://www.usantidoping.org/prohibited_sub/list.asp.
18. USADA guide to prohibited classes of substances and prohibited methods of doping. Retrieved October 2001, from http://www.usantidoping.org/prohibited_sub/guide.asp.
19. Gifford RW Jr. Antihypertensive therapy. Angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, and calcium antagonists. Med Clin North Am 1997;81:1319-33.
20. Chick TW, Halperin AK, Gacek EM. The effect of antihypertensive medications on exercise performance: a review. Med Sci Sports Exerc 1988;20:447-54.
21. Freis ED. Current status of diuretics, beta-blockers, alpha-blockers, and alpha-beta-blockers in the treatment of hypertension. Med Clin North Am 1997;81:1305-17.
22. Amery A, Birkenhager W, Brixko, Bulpitt C, Clement D, Deruyttere M, et al. Mortality and morbidity results from the European Working Party on High Blood Pressure in the Elderly trial. Lancet 1985;1(8442):1349-54.
23. Dahlof B, Lindholm LH, Hansson L, Schersten B, Ekbom T, Wester PO. Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension). Lancet 1991;338:1281-5.
24. Medical Research Council trial of treatment of hypertension in older adults: principal results. MRC Working Party. BMJ 1992;304:405-12.
25. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group. JAMA 1991;265:3255-64.
26. Pahor M, Shorr RI, Somes FW, Cushman WC, Ferrucci L, Bailey JE, et al. Diuretic-based treatment and cardiovascular events in patients with mild renal dysfunction enrolled in the Systolic Hypertension in the Elderly Program. Arch Intern Med 1998;158:1340-5.
27. Philipp T, Anlauf M, Distler A, Holzgreve H, Michaelis J, Wellek S. Randomised, double blind, multicentre comparison of hydrochlorothiazide, atenolol, nitrendipine, and enalapril in antihypertensive treatment: results of the HANE study: HANE Trial Research Group. BMJ 1997;315:154-9.
28. Curb JD, Pressel SL, Cutler JA, Savage PJ, Applegate WB, Black H, et al. Effect of diuretic-based antihypertensive treatment on cardiovascular disease risk in older diabetic patients with isolated systolic hypertension. Systolic Hypertension in the Elderly Program Cooperative Research Group. JAMA 1996;276:1886-92.
29. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the Antihypertensives and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). ALLHAT Collaborative Research Group. JAMA 2000;283:1967-75.
30. Lund-Johansen P. Haemodynamics in essential hypertension. Clin Sci [Colch] 1980;59(suppl 6): S343-54.