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Master's Thesis

**HYPERTENSION AS A MEDICAL AND SOCIAL PROBLEM AND WAYS TO
SOLVE IT**

Master of Science in Nursing

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Master thesis abstract

HYPERTENSION AS A MEDICAL AND SOCIAL PROBLEM AND WAYS TO SOLVE IT

the purpose

Hypertension, or high blood pressure, is a serious pathological condition that significantly increases the risk of developing diseases of the cardiovascular system, brain, kidneys, and other diseases. Hypertension is also one of the leading causes of death worldwide. The role of a nurse in improving hypertension control has expanded over the past 50 years, complementing the role of a doctor. Today, the roles of practicing nurses in the management of hypertension include all aspects of treatment, including detection, referral to specialists, and follow-up; diagnosis and drug treatment; patient education, counseling, and skills development; care coordination; clinic or office management.

methods

With the help of this scientific study, the epidemiology, etiology and pathogenesis of arterial hypertension, the classification and clinic of arterial hypertension were studied, the features of the treatment of patients with arterial hypertension in certain clinical situations were investigated, urgent conditions against the background of a pronounced increase in blood pressure were investigated, and the features of medical rehabilitation, dispensary supervision, primary and secondary prevention of hypertension were studied.

Findings

Medical staff should remember that there is no need to quickly reduce blood pressure to "normal numbers" (especially in acute stroke). Stroke patients require a special approach, because excessive and/or rapid decrease in blood pressure can lead to an increase in cerebral ischemia. In most other cases, doctors are recommended to ensure a rapid, but no more than 25% of the initial values, reduction in blood pressure for the first 2 hours from the moment of admission to the hospital.

For all patients with hypertension, it is recommended to develop an individual rehabilitation plan, which includes recommendations for achieving the target BP, self-monitoring of BP, increasing adherence to treatment, nutrition, physical activity, weight control. In order to reduce the risk of cardiovascular complications, all patients with hypertension are recommended at least 150 minutes (2 hours 30 minutes) per week of moderate-intensity aerobic physical activity or 75 minutes (1 hour 15 minutes) per week of high-intensity aerobic physical activity.

Dynamic monitoring is an extremely important component of medical care for patients with hypertension, whose tasks are: maintaining target blood pressure levels, monitoring the implementation of medical recommendations for correcting risk factors, monitoring compliance with the antihypertensive therapy regimen, assessing the condition of target organs.

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INTRODUCTION

Relevance of the study. Despite significant progress in the prevention and treatment of many heart diseases [5, 8, 15, 41, 45, 57], in recent decades, arterial hypertension or hypertensive disease [2, 143, 24] as a medical and social problem remains in the first positions on the need to solve it in the shortest possible time [31, 61, 62].

Hypertension among a variety of cardiovascular diseases is becoming an increasingly common pathology [22, 25] and to date has acquired the scale of a "non-infectious epidemic" [22, 61].

The main facts of WHO [61, 62] concerning hypertension indicate that, according to experts, 1.28 billion adults aged 30-79 years worldwide are hypertensive, of which the majority (two thirds) live in low- and middle-income countries.

According to experts, 46% of adults with hypertension are unaware of the presence of the disease. Less than half (42%) of adult patients suffering from hypertension are diagnosed [40, 46, 54, 55] and are being treated [10, 36]. Approximately one in five adult hypertensive patients, which is approximately 21%, controls this disease [42, 52, 63].

Hypertension [21, 22, 26, 27, 47], or high blood pressure [6, 13], a serious pathological condition that significantly increases the risk of developing diseases of the cardiovascular system [4, 11, 12, 19, 35], brain, kidneys [9, 32, 34, 53, 65] and other diseases [8, 24, 25, 26, 64]. Hypertension is also one of the leading causes of death worldwide [7, 14, 16, 33, 44, 53, 56].

Reducing the prevalence of hypertension by 33% in the period from 2010 to 2030 is among the global goals in the fight against noncommunicable diseases. Hypertension and cardiovascular diseases will remain in the XXI century the most urgent health problem in most countries of the world, despite the continuous improvement of methods of diagnosis and treatment of cardiac patients [17, 22, 25, 38, 50, 57].

To date, among the population that suffers from cardiovascular diseases, the most common are hypertension [21, 26], cerebrovascular diseases and coronary heart disease [3, 25, 30]. Unfortunately, the number of children and adolescents with high blood pressure is growing.

Arterial hypertension is not called a "silent killer" for nothing, because it often proceeds asymptotically, but plays an important role in the development of severe complications leading to death [53, 56], such as acute myocardial infarction, progressive angina, stroke, acute and chronic heart failure, thromboembolism in various organs and others. In patients with arterial hypertension, an increase in total mortality was revealed by 5 times [7, 16, 33].

The role of a nurse in improving hypertension control has expanded over the past 50 years [23], complementing the role of a doctor [2]. Nurse involvement began with blood pressure measurement and monitoring [42, 52] and patient education and has expanded to become one of the most effective strategies [31, 39, 63] to improve blood pressure control. Today, the roles of practicing nurses in the management of hypertension include all aspects of treatment, including detection, referral to specialists and follow-up; diagnosis and drug treatment; patient education, counseling and skills development; care coordination; clinic or office management;

public health management; and measuring the effectiveness of care and improving its quality.

A multidisciplinary team focused on the patient [2, 23] is a key feature of effective models of care [63], which have been found to improve the processes of care and monitor indicators. In addition to their clinical role, nurses lead clinical and community-based research aimed at bridging the gap in hypertension quality and ethnic differences through a comprehensive study of the social, cultural, economic and behavioral determinants of hypertension outcomes and the development of culturally sensitive interventions aimed at addressing these determinants and risk factors [22, 28, 29, 49, 55, 58].

Taking into account the medical and social significance of this problem for the whole society, patients and nursing staff [2, 23], the organization of care for patients with hypertension, management of this disease [3, 43, 63], timely prevention of hypertension and its complications [40, 56], prediction of hypertension [56] are a very responsible task and require scientific research.

The purpose of the study: to study and investigate the features of the epidemiology, etiology and pathogenesis of arterial hypertension, its classification and clinic, as well as to study the features of the treatment of patients with hypertension in certain clinical situations and emergency conditions against the background of a pronounced increase in blood pressure.

Research tasks.

1. To study the epidemiology, etiology and pathogenesis of arterial hypertension.
2. To study the classification and clinic of arterial hypertension.
3. To investigate the features of the treatment of patients with arterial hypertension in certain clinical situations.
4. To investigate urgent conditions against the background of a pronounced increase in blood pressure.
5. To study the features of medical rehabilitation, dispensary supervision, primary and secondary prevention of hypertension.

The object of the study. Patients with arterial hypertension, as well as with arterial hypertension in combination with certain diseases, patients with urgent conditions on the background of a pronounced increase in blood pressure.

The subject of the study. Epidemiology, etiology and pathogenesis, classification and clinic of arterial hypertension; principles and features of treatment of patients with arterial hypertension in certain clinical situations; features of emergency conditions against the background of a pronounced increase in blood pressure, features of medical rehabilitation, dispensary supervision, primary and secondary prevention of hypertension.

Research methods: bibliosemantic method, analytical method, general clinical and special general therapeutic methods of examination of the patient, life and disease history, risk assessment and presence of hypertension, observation, objective examination, assessment of the general condition of the patient, collection of information about the main complaints, laboratory and instrumental research methods (complaints and anamnesis, physical examination, laboratory diagnostics, instrumental diagnostics, other diagnostic studies: assessment of cognitive function using the MMSE (Mini Mental State Examination) test, complex laboratory tests, in particular the "Arterial hypertension laboratory panel",

Scientific and practical significance of the study. With the help of this scientific study, the epidemiology, etiology and pathogenesis of arterial hypertension, the classification and clinic of arterial hypertension were studied, the features of the treatment of patients with arterial hypertension in certain clinical situations were investigated, urgent conditions against the background of a pronounced increase in blood pressure were investigated, and the features of medical rehabilitation, dispensary supervision, primary and secondary prevention of hypertension were studied.

CHAPTER 1
EPIDEMIOLOGY, ETIOLOGY AND PATHOGENESIS, CLASSIFICATION
AND CLINICAL PICTURE ARTERIAL HYPERTENSION
(LITERATURE REVIEW)

1.1. Epidemiology of arterial hypertension

The prevalence of arterial hypertension (AH) among the adult population is 30-45% [22, 25]. The prevalence of hypertension does not depend on income level and is the same in low-, middle- and high-income countries. Among men aged 25-65, the prevalence of hypertension is slightly higher (in some regions it reaches 47%), while among women the prevalence of hypertension is about 40% [25]. The prevalence of hypertension increases with age, reaching 60% and higher in people over 60 years of age. Since the observed increase in life expectancy is accompanied by an aging population and, accordingly, an increase in the number of sedentary overweight patients [4], it is predicted that the prevalence of hypertension will increase worldwide [56]. According to the forecast, by 2025 the number of patients with hypertension will increase by 15-20% and reach almost 1.5 billion people [56, 61, 62].

In general, 26.4% of the adult population in 2000 had hypertension (26.6% of men and 29.2% of women), according to forecasts, 29.0% of men and 29.5% of women will have this condition by 2025. It is estimated that the total number of adults with hypertension in 2000 was 972 million; 333 million in economically developed countries and 639 million in economically developing countries. According to forecasts, the number of adults with hypertension in 2025 will increase by about 60% and will total 156,000,000 people.

Hypertension is a leading risk factor for the development of cardiovascular diseases: myocardial infarction (MI), stroke, coronary heart disease (CHD), chronic

heart failure (CHF)), cerebrovascular (ischemic or hemorrhagic stroke, transient ischemic attack) and renal diseases [3041, 50, 53, 65].

There is a correlation between increased blood pressure and the risk of cardiovascular, cerebrovascular and renal complications. Elevated blood pressure is the main factor in the development of premature death and the cause of almost 10 million deaths and more than 200 million cases of disability in the world [7, 16, 33]. The level of systolic blood pressure (SBP) greater than 140 mmHg is associated with an increased risk of mortality and disability in 70% of cases, while the largest number of deaths during the year associated with the level of SBP occur due to coronary artery disease, ischemic and hemorrhagic strokes [12, 19, 55, 58]. There is a direct link between the blood pressure level and the risk of cardiovascular diseases. This relationship begins with relatively low values – 110-115 mmHg for SAD and 70-75 mmHg for diastolic blood pressure (DBP) [2, 24, 47].

Elevated blood pressure levels measured in or out of a medical facility have a direct and independent relationship with the frequency of most cardiovascular events, namely hemorrhagic stroke, ischemic stroke, MI, sudden death, heart failure (HF) and peripheral artery disease, as well as terminal renal failure [9, 32, 34]. More and more data indicate a close association of hypertension with an increase in the frequency of atrial fibrillation [30], as well as cognitive dysfunction and dementia. An increase in blood pressure in middle age is associated with the development of cognitive impairment and dementia in old age, and intensive therapy of hypertension with the achievement of target blood pressure figures reduces the risks of moderate cognitive impairment and possible dementia.

A direct link between elevated blood pressure and the risk of cardiovascular events has been scientifically confirmed for all age and ethnic groups. In patients over 50 years of age, SAD is a stronger predictor of events than DAD [21, 27]. High DBP is associated with an increased risk of cardiovascular events and is more often elevated in younger (less than 50 years old) patients. DAD tends to decrease in the second half of life due to increased arterial stiffness, while SAD, as a risk factor, becomes even more

important during this period [2, 3, 24]. In middle-aged and elderly patients, an increase in pulse pressure, which is the difference between SAD and DAD, has an additional negative impact on the prognosis [42, 56].

1.2. Definition of arterial hypertension

Arterial hypertension (AH) is a syndrome of increased systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg. [2, 13, 21, 24, 27, 47].

Hypertension is a chronically occurring disease, the main manifestation of which is an increase in blood pressure, not associated with the identification of obvious causes leading to the development of secondary forms of hypertension (symptomatic hypertension). The term "hypertension", proposed by G. F. Lang in 1948, corresponds to the terms "essential hypertension" and "arterial hypertension" used in many countries. Hypertension prevails among all forms of hypertension, its prevalence exceeds 90%.

Secondary (symptomatic) arterial hypertension is hypertension caused by a known cause that can be eliminated with appropriate intervention.

Hypertensive crisis (GC) is a condition caused by a significant increase in blood pressure, associated with acute damage to target organs, often life-threatening, requiring immediate qualified actions aimed at reducing blood pressure, usually with the help of intravenous therapy.

1.3. Etiology and pathogenesis of arterial hypertension

The etiology of arterial hypertension remains not fully elucidated, but a number of factors have been identified that are closely and independently associated with an increase in blood pressure:

- age – an increase in age is associated with an increase in the frequency of hypertension and blood pressure (primarily systolic) [6, 13];

- overweight and obesity contribute to an increase in blood pressure;
- hereditary predisposition – an increase in blood pressure occurs approximately 2 times more often among people whose one or both parents had arterial hypertension. Epidemiological studies have shown that about 30% of BP variations in different populations are due to factors:

- excessive sodium intake (>5 g/day) [1, 20, 51];
- alcohol abuse, smoking [29];
- genetic factors [11];
- physical inactivity [28].

A persistent and prolonged increase in blood pressure is due to a change in the ratio of three hemodynamic parameters:

- an increase in total peripheral vascular resistance;
- increased cardiac output (minute volume);
- an increase in the volume of circulating blood.

The most important pathogenetic links in the formation and progression of essential hypertension (GB) are [3, 21, 26, 27, 59, 60]:

- activation of the sympatho-adrenal system (implemented mainly through alpha and beta adrenergic receptors);
- activation of the renin-angiotensin-aldosterone system; including an increase in the production of mineralocorticoids (aldosterone, etc.), initiated, in particular, by hyperactivation of the renal renin-angiotensin-aldosterone system;
- disruption of membrane transport of cations (Na^+ , Ca^{2+} , K^+);
- increased sodium reabsorption in the kidneys;
- endothelial dysfunction with predominance of vasoconstrictor substances (tissue angiotensin II, endothelin) and decreased production of depressant compounds (bradykinin, NO, prostacyclin, etc.);
- structural changes in the vascular wall of the arteries of the muscular (resistive) and elastic type, including due to low-intensity non-infectious inflammation;
- violation of microcirculation (decrease in capillary density);

- violation of the baroreceptor link of the central blood pressure regulation system;

- increased stiffness of large vessels.

Since blood pressure corresponds to cardiac output (CB) \times total peripheral vascular resistance, pathogenetic mechanisms should include:

- Increased cardiac output;
- Increased total peripheral vascular resistance;
- Both.

In most patients, cardiac output is normal or slightly elevated and overall peripheral vascular resistance is increased. This model is typical for primary arterial hypertension, as well as for hypertension caused by primary hyperaldosteronism, pheochromocytoma, renovascular disease and parenchymal kidney diseases.

In other patients, cardiac output increases (possibly due to venoconstriction in large veins), and the total peripheral vascular resistance does not correspond to an increase in cardiac output and is normal. In the future, the total peripheral vascular resistance increases and cardiac output normalizes, probably due to self-regulation. Some diseases that increase cardiac output (thyrotoxicosis, arteriovenous fistula, aortic insufficiency), especially when the stroke volume increases, can cause isolated systolic hypertension.

Some elderly patients have isolated systolic hypertension with normal or low cardiac output, probably due to the stiffness of the aorta and its main branches. In patients with high, persistent diastolic pressure, cardiac output is often reduced.

Plasma volume tends to decrease as blood pressure increases; rarely plasma volume remains normal or increases. Plasma volume, as a rule, is increased in primary aldosteronism or parenchymal kidney diseases, may be it is sufficiently reduced in arterial hypertension caused by pheochromocytoma.

Renal blood flow gradually decreases as diastolic blood pressure increases, and arteriosclerosis begins. The glomerular filtration rate remains normal until disturbances occur during the development of the disease; as a result, the filtration fraction

increases. Coronary, cerebral and muscular blood flow is maintained until the development of severe atherosclerosis in these vascular basins.

Pathological sodium transfer. For many causes of hypertension, sodium transport through the cell wall is disrupted due to damage or inhibition of the potassium-sodium pump (Na^+ , K^+ -ATPase) or increased permeability of cells with sodium ions. The result is an increase in the content of intracellular sodium, which makes the cells more sensitive to sympathetic stimulation. Calcium follows sodium, so the accumulation of intracellular calcium can lead to hypersensitivity.

Since Na^+ , K^+ -ATPase can move norepinephrine back into sympathetic neurons (thus inactivating this neurotransmitter), inhibition of this mechanism can also enhance the effect of norepinephrine by increasing blood pressure. Defects in sodium transport can be observed in children with normal blood pressure, whose parents suffer from hypertension.

Sympathetic nervous system. Sympathetic stimulation increases blood pressure; as a rule, it occurs more often in patients with high blood pressure and hypertension than in patients with normal pressure. It is unknown whether this hyperreactivity is present in the sympathetic nervous system or in the myocardium and vascular smooth muscles. High resting heart rate, which it may be the result of increased activity of the sympathetic nervous system, is a well-known predictor of arterial hypertension. In some patients with hypertension, the level of catecholamines circulating in plasma at rest is higher than usual.

The renin-angiotensin-aldosterone system helps regulate blood volume and, consequently, blood pressure. Renin— an enzyme formed in the juxtaglomerular apparatus, catalyzes the conversion of angiotensinogen into angiotensin I. Angiotensin-converting enzyme (ACE) cleaves this inactive product mainly in the lungs, but also in the kidneys and brain, to angiotensin II, a highly active vasoconstrictor that also stimulates the autonomic centers in the brain, increasing discharges in the sympathetic nerve and stimulating the release of aldosterone and vasopressin.

Aldosterone and vasopressin cause sodium and water retention, increasing blood pressure. Aldosterone also increases potassium excretion; low plasma potassium (< 3.5 mEq/L) increases vasoconstriction through the closure of potassium channels. Angiotensin III, present in the bloodstream, stimulates the release of aldosterone as actively as angiotensin II, but has much less vasoconstrictive activity. Since the enzyme chymase also converts angiotensin I to angiotensin II, ACE inhibiting drugs do not completely suppress angiotensin II production.

Renin secretion is controlled by at least 4 mechanisms that are not mutually exclusive:

- The renal vascular receptor responds to changes in pressure in the wall of the afferent arteriole;
- The dense spot receptor detects changes in the flow rate or concentration of sodium chloride in the distal tubules;
- Circulating angiotensin affects renin secretion through a negative feedback mechanism;
- The sympathetic nervous system stimulates renin secretion mediated via beta receptors via the renal nerve.

Angiotensin is usually responsible for the development of renovascular hypertension, at least at the initial stage, but the role of the renin-angiotensin-aldosterone system in primary arterial hypertension has not been established. However, in African Americans with hypertension, renin levels are usually low. Elderly patients also tend to have low angiotensin II levels.

Arterial hypertension due to chronic parenchymal kidney diseases (renal hypertension) is the result of a combination of renin-dependent and volume-dependent mechanisms. In most cases, an increase in renin activity is not detected in peripheral blood. Arterial hypertension, as a rule, has a moderate stage and is sensitive to the balance of sodium and water [1, 20, 51].

Lack of vasodilators. A lack of vasodilators (for example, bradykinin, nitric oxide) rather than an excess of vasoconstrictors (for example, angiotensin, norepinephrine) can lead to hypertension.

A decrease in the level of nitric oxide due to arterial rigidity is associated with salt-sensitive hypertension, an excessive increase in systolic blood pressure by more than 10-20 mmHg after a heavy load of sodium (for example, eating Chinese food). Diet is of great importance for the prevention and treatment of hypertension [18, 51].

If the kidneys do not produce enough vasodilators (due to parenchymal kidney disease or bilateral nephrectomy), blood pressure may increase.

Vasodilators and vasoconstrictors (mainly endothelin) are also produced by endothelial cells. Thus, endothelial dysfunction strongly affects the level of blood pressure.

1.4. Classification of arterial hypertension

Arterial hypertension is classified according to the degree, which is determined by the level of blood pressure in untreated patients; the stage, which is determined by the presence of diabetes mellitus [8, 24, 64], damage to target organs and associated clinical conditions; the risk category of cardiovascular complications, which takes into account the level of blood pressure, concomitant risk factors, the presence of diabetes mellitus, defeat target organs, associated clinical conditions.

The blood pressure category is determined by the results of its three-fold measurement in the patient's sitting position. Use the average values of SAD and DAD, determined in the last two measurements. Arterial hypertension is classified into grades 1, 2 or 3, depending on the value of SAD. If the values of SAD and DAD fall into different categories, then the degree of arterial hypertension is estimated by a higher category.

The isolation of the 3 stages of arterial hypertension is based on the presence of target organ damage, associated clinical conditions, diabetes mellitus and chronic

kidney disease. The stage of hypertension does not depend on the level of blood pressure.

3 GB stages are allocated.

Stage I – absence of target organ damage and associated clinical conditions, possible presence of risk factors.

Cardiovascular risk factors in patients with arterial hypertension: gender (men > women); age ≥ 55 years in men, ≥ 65 years in women; smoking (present or past; smoking in the past should be considered as risk factors when quitting smoking during the last year); dyslipidemia (each of the presented indicators of lipid metabolism is taken into account): total cholesterol > 4.9 mmol/L and/or low-density lipoprotein cholesterol (LDL-C) > 3.0 mmol/L and/or high-density lipoprotein cholesterol (HDL-C) in men – < 1.0 mmol/l (40 mg/dl), in women – < 1.2 mmol/l (46 mg/dl) and/or triglycerides > 1.7 mmol/l; uric acid (≥ 360 mmol/l in women, ≥ 420 mmol/l in men); violation fasting glycemia: fasting plasma glucose 5.6-6.9 mmol/l; impaired glucose tolerance; overweight (body mass index (BMI) 25-29.9 kg/m²) or obesity (BMI ≥ 30 kg/m²); family history of cardiovascular diseases at a young age (< 55 years for men and < 65 years for women); development of hypertension at a young age in parents or in the family; early menopause; sedentary lifestyle; psychological and socio-economic factors; resting heart rate > 80 beats/min.

Stage II implies the presence of asymptomatic target organ damage associated with hypertension and/or chronic kidney disease ((GFR) 30-59 ml/min), and/or DM without target organ damage and assumes the absence of associated clinical conditions.

Asymptomatic lesion of target organs:

- Arterial stiffness:

Pulse pressure (in elderly patients) ≥ 60 mmHg,

Carotid-femoral pulse wave velocity > 10 m/s;

- Electrocardiographic (ECG) signs of left ventricular hypertrophy (Sokolov-Lyon index > 35 mm, or the amplitude of the R wave in the aVL lead ≥ 11 mm, Cornell voltage index > 28 mm for men and > 20 mm for women);

- Echocardiographic signs of left ventricular hypertrophy (left ventricular mass index, especially for overweight and obese patients; indexing to body surface area (left ventricular mass/height, m²) for patients with normal body weight: >115 g/m² (men) and >95 g/m² (women));
- Albuminuria 30-300 mg/24 h or albumin-creatinine ratio 30-300 mg/g or 3.4-34 mg/mmol (preferably in the morning urine portion);
- Stage 3 chronic kidney disease with GFR >30-59 ml/min/1.73 m²;
- Ankle-shoulder index (LPI) <0.9;
- Severe retinopathy: the presence of hemorrhages, exudates or swelling of the nodule of the optic nerve.

Stage III is determined by the presence of associated clinical conditions, including chronic kidney disease C4-C5 stages, and/or diabetes mellitus with target organ damage.

Diabetes mellitus (considered as an additional condition aggravating the risk) [8, 24, 64]: fasting plasma glucose ≥ 7.0 mmol/L with two consecutive measurements and/or glycated hemoglobin (HbA1c) $\geq 6.5\%$, and/or plasma glucose after exercise or with random determination ≥ 11.1 mmol/L.

The stages of hypertension have a clarifying character for the defeat of target organs and concomitant pathology.

Based on the blood pressure level, the presence of risk factors, target organ damage, associated clinical conditions, diabetes mellitus, 4 risk categories of cardiovascular complications are distinguished. The most significant is the determination of the risk category in patients with stage I and II GB.

1.5. Clinical picture of arterial hypertension

In most cases, blood pressure increases asymptotically, and arterial hypertension is detected only during an objective examination of the patient. In cases

where there are complaints, they are non-specific (headache, dizziness, palpitations, etc.) [26, 47].

Arterial hypertension usually proceeds asymptotically until complications develop in the target organs. Uncomplicated hypertension can cause dizziness, redness of the face, headache, fatigue, nosebleeds and increased excitability. Severe hypertension (hypertensive crisis) can cause serious cardiovascular, neurological, renal symptoms and retinal damage (for example, symptomatic atherosclerosis of the coronary arteries, heart failure, hypertensive encephalopathy, renal failure).

The presence of the 4th heart tone is one of the earliest signs of hypertensive cardiomyopathy.

Retinal changes may include narrowing of arterioles, hemorrhages, exudation and edema of the optic disc in patients with encephalopathy (hypertensive retinopathy). The changes are classified (according to the Keith-Wagener-Barker classification) into 4 groups (in order of deterioration of the forecast):

- Stage 1: Narrowing of arterioles only
- Stage 2: Narrowing and sclerosis of arterioles
- Stage 3: Hemorrhages and exudates in addition to vascular changes
- Stage 4: Edema of the optic disc

At the early stage of arterial hypertension, no pathological changes are observed. Severe or prolonged arterial hypertension damages target organs (primarily the cardiovascular system, brain, kidneys), increasing the risk of developing:

- Coronary heart disease (CHD) and myocardial infarction (MI)
- Heart failure
- Stroke (especially hemorrhagic)
- Kidney failure

The mechanism includes the development of generalized arteriosclerosis and the acceleration of atherogenesis. Arteriosclerosis is characterized by medial hypertrophy, hyperplasia and hyalinization, this is especially pronounced in small arterioles, in particular in the eyes and kidneys. In the kidneys, changes narrow the

lumen of the arterioles, thus leading to even more pronounced arterial hypertension. In addition, after the initial narrowing of the arteries, any slight additional contraction of already hypertrophied smooth muscles reduces the lumen to a greater extent than with a normal diameter of the artery. These factors may explain why the duration of arterial hypertension is inversely proportional to the success of specific treatment (for example, renovascular surgery) of secondary causes for the restoration of normal blood pressure [5, 6, 13, 27].

Due to increased afterload, the left ventricle gradually hypertrophs, which leads to diastolic dysfunction. The left ventricle eventually expands [3], which leads to dilated cardiomyopathy and heart failure with systolic dysfunction and often aggravated by atherosclerotic heart disease. Dissection of the thoracic aorta, as a rule, is a consequence of arterial hypertension; almost all patients with abdominal aortic aneurysm have arterial hypertension [21].

In symptomatic hypertension, complaints are caused by the underlying disease:

- Obstructive sleep apnea syndrome (OSA, "sleep respiratory arrest disease"): snoring, headache in the morning, daytime drowsiness, impaired memory, attention, inadequate night sleep;
- Primary hyperaldosteronism: muscle weakness, polyuria, polydipsia, constipation;
- Pheochromocytoma: paroxysmal hypertension, headache, profuse sweating, palpitations, labile increase in blood pressure, orthostatic hypotension;
- Itsenko-Cushing syndrome: moon-shaped face, plethora, fatty hump, hirsutism, central obesity, skin atrophy, purple striae, bruises, carbohydrate metabolism disorders;
- Thyroid diseases: symptoms of thyrotoxicosis or hypothyroidism;
- Aortic coarctation: headache, cold limbs, leg pain during exercise, nosebleeds.

In general, it should be emphasized that hypertension is an important public health problem worldwide [61, 62]. Prevention, detection, treatment and control of this condition should be a priority for solving important medical and social problems of society.

CHAPTER 2 OBJECT AND METHODS OF RESEARCH

The object of the study was 289 patients with arterial hypertension, as well as with arterial hypertension in combination with certain diseases, among which there were patients with urgent conditions on the background of a pronounced increase in blood pressure.

In the study of all patients, general clinical and special general therapeutic methods of examination of the patient, life and disease history, risk assessment and presence of hypertension, observation, objective examination, assessment of the general condition of the patient, collection of information about the main complaints, laboratory and instrumental research methods were used

Examinations of patients with arterial hypertension included:

- 1). Complaints and anamnesis
- 2). Physical examination
- 3). Laboratory diagnostics
- 4). Instrumental diagnostics
- 5). Other diagnostic studies: assessment of cognitive function using the MMSE test (Mini Mental State Examination), complex laboratory tests, in particular "Arterial hypertension laboratory panel", "Blood tests in hypertension" (Panel of the laboratory of arterial hypertension, Blood tests for hypertension).

- 1). Complaints and anamnesis

Many patients with elevated blood pressure may not have any complaints. Symptoms (headaches, shortness of breath, chest pain, nosebleeds, subjective dizziness, swelling, visual impairment, feeling of heat, sweating, hot flashes) that occur in hypertension are nonspecific and can be observed in other diseases.

In the presence of these symptoms in any patient, it is necessary to take into account the possibility of diagnosed hypertension during his examination.

It is recommended to collect a complete medical and family history to assess family predisposition to hypertension and cardiovascular diseases.

2). Physical examination

All patients with hypertension are recommended to determine anthropometric data to detect overweight /obesity, assessment of neurological status and cognitive function, fundus examination to detect hypertensive retinopathy, palpation and auscultation of the heart and carotid arteries, palpation and auscultation of peripheral arteries to detect pathological noises, comparison of blood pressure between hands at least once.

All patients with hypertension are recommended to palpate the pulse at rest to measure its frequency and rhythmicity in order to detect arrhythmias.

3). Laboratory diagnostics

To establish the diagnosis of hypertension, laboratory diagnostics is not required, but it is necessary in order to exclude secondary forms of hypertension, assess cardiovascular risk, and concomitant pathology affecting the effectiveness of treatment and the quality of life of the patient.

In order to exclude secondary hypertension, all patients with hypertension are recommended to conduct a general (clinical) blood test (hemoglobin / hematocrit, leukocytes, platelets).

All patients with hypertension are recommended to study serum creatinine levels and calculate GFR in ml/min/ 1.73 m² according to the formula Chronic Kidney Disease Epidemiology (CKD-EPI) in special calculators to identify renal dysfunction and assess cardiovascular risk. It is performed in all patients with hypertension due to the fact that kidney damage is a significant prognostic factor in hypertension, the presence of a proven link between the detection of albuminuria and increased cardiovascular mortality. Daily urinary albumin excretion ≥ 30 mg/day. It is associated with an increased risk of CKD complications. In the meta-analysis of the Consortium for the prognosis of CKD, associations were found between the daily excretion of albumin ≥ 30 mg/day. In the study, the test strips, with the risk of general mortality and

mortality from cardiovascular diseases, renal failure, progression of CKD in the general population and in populations with an increased risk of developing cardiovascular diseases. The ratio of albumin / creatinine in urine (preferably in the morning portion) is 30-300 mg / g; 3.4-34 mg / mmol is a marker of kidney damage.

To stratify the risk and identify lipid metabolism disorders, it is recommended to study the level of OHC, HDL-C, LDL-C (direct measurement or calculated) and TG in the blood for all patients with hypertension.

All patients with hypertension are recommended to study the level of potassium and sodium in the blood to identify electrolyte disorders and differential diagnosis with secondary hypertension.

It is performed in all patients with hypertension to detect electrolyte disturbances due to the proven relationship between serum potassium and sodium levels and blood pressure levels.

All patients with hypertension are recommended to study the level of uric acid in the blood to detect hyperuricemia.

It is performed in all patients with hypertension due to the fact that the level of uric acid is a significant prognostic factor in hypertension, as well as the presence of a proven link between hyperuricemia and increased cardiovascular mortality.

4). Instrumental diagnostics

Carrying out instrumental diagnostic methods is necessary to exclude secondary forms of hypertension, identify target organ damage, assess cardiovascular risk, and concomitant pathology affecting the effectiveness of treatment and the quality of life of the patient.

A 12-channel ECG is recommended for all patients with hypertension to detect left ventricular hypertrophy and determine cardiovascular risk.

Despite the fact that ECG is a less sensitive method of diagnosing left ventricular hypertrophy compared to EchoCG, it is indispensable for documenting heart rate, heart rate and detecting arrhythmias.

In patients with hypertension, in the presence of ECG changes or symptoms/signs of left ventricular dysfunction, EchoCG is recommended to detect the degree of left ventricular hypertrophy.

Patients with hypertension in combination with cerebrovascular disease or signs of atherosclerotic vascular lesions of other localizations, with a history of transient weakness in the extremities on one side or numbness of half of the body, as well as men over 40 years old, women over 50 years old and patients with high overall cardiovascular risk, duplex scanning of brachiocephalic arteries is recommended to detect atherosclerotic plaques/stenoses of internal carotid arteries.

All patients with impaired renal function, albuminuria and suspected secondary hypertension are recommended to perform ultrasound of the kidneys and duplex scanning of the renal arteries in order to assess the size, structure, as well as the presence of congenital anomalies of the kidneys or renal artery stenosis.

Patients with hypertension of 2-3 levels, all patients with diabetes mellitus and hypertension are recommended to conduct an examination of the fundus by an ophthalmologist (hemorrhages, exudates, swelling of the nipple of the optic nerve) to detect hypertensive retinopathy.

Hypertensive retinopathy, detected by fundoscopy (examination of the fundus), has a high prognostic significance in hypertension. The detection of retinal hemorrhages, microaneurysms, solid exudates, papilloedema indicates severe hypertensive retinopathy and significantly correlates with a poor prognosis. The changes characteristic of the early stages of retinopathy have no significant prognostic value and are characterized by low reproducibility.

Patients with hypertension in the presence of neurological symptoms and /or cognitive impairments are recommended to perform computed tomography (CT) or magnetic resonance imaging (MRI) of the brain to exclude cerebral infarctions, microbleeds and white matter damage and other pathological formations.

5). Other diagnostic studies

Other diagnostic studies are not provided as part of the diagnosis of hypertension, it is possible to expand diagnostic studies by the decision of a doctor, depending on the clinical situation and the patient's condition. Cognitive impairment in elderly patients is partially associated with hypertension, and therefore, in elderly patients with a history suggesting early cognitive deficits, an assessment of cognitive function using the MMSE (Mini Mental State Examination) test is recommended.

Our study also used comprehensive laboratory tests, in particular the "Arterial hypertension laboratory panel", "Blood tests in hypertension" (Panel of the Arterial hypertension Laboratory, Blood tests for hypertension).

Venous blood should be used for this study.

It is necessary to properly prepare for the study, namely:

- Exclude alcohol from the diet within 24 hours before the study.
- Do not eat for 12 hours before the study, you can drink pure still water.
- Completely exclude (in consultation with the doctor) taking medications within 24 hours before the study.
- Eliminate physical and emotional stress for 30 minutes before the study.
- Do not smoke for 30 minutes before the study.

When examining a patient with newly diagnosed arterial hypertension, a complex of laboratory tests is performed. A thorough laboratory examination is especially necessary when arterial hypertension occurs at a young or elderly age, in the presence of symptoms indicating secondary arterial hypertension (for example, the detection of noise during auscultation of renal vessels or the episodic nature of an increase in blood pressure with pheochromocytoma), as well as with a rapidly progressive and persistent course of the disease against the background of adequate hypotensive therapy.

A comprehensive laboratory examination includes blood counts that exclude the main causes of secondary arterial hypertension:

- Kidney diseases. A common cause of arterial hypertension in children are parenchymal kidney diseases (glomerulonephritis, congenital malformations, reflux

nephropathy), in young women - fibromuscular hyperplasia of the renal artery, in elderly patients - atherosclerosis of the renal artery. To exclude kidney diseases as a cause of secondary arterial hypertension, creatinine levels are examined. Creatinine is a good indicator of glomerular filtration rate (GFR) and overall kidney function. A specific sign of renal artery damage is a rapid and significant increase in blood creatinine levels when ACE inhibitors are prescribed (an increase of more than 0.5-1 mg / dl).

- Hyperaldosteronism caused by adenoma or bilateral hyperplasia of the adrenal cortex is more typical for middle-aged patients (40-64 years). Recently, it has become clear that hyperaldosteronism is more common than previously estimated, and can be the cause of hypertension in at least 6% of cases. To exclude hyperaldosteronism, potassium and sodium are studied. Primary hyperaldosteronism is characterized by hypokalemia and hypernatremia. It should be noted that a violation of the concentration of these electrolytes is observed only in 30% of patients with primary hyperaldosteronism. For a more accurate diagnosis of this condition, it is recommended to study the concentration of aldosterone and renin and evaluate their ratio.

- Arterial hypertension can be observed in diseases of the thyroid gland, occurring with both hyperthyroidism and hypothyroidism. Hyperthyroidism as a cause of arterial hypertension is more common in patients aged 20-50 years, while hypothyroidism – in elderly patients (over 60 years). To assess the function of the thyroid gland, the level of thyroid-stimulating hormone TSH and free thyroxine T4 are examined. hyperthyroidism is characterized by an increase in T4 and a decrease in TSH. Hypothyroidism is characterized by a decrease in T4 and an increase in TSH.

- Other, more rare, causes of secondary arterial hypertension include blood diseases, including anemia and polycythemia. To exclude these conditions, a general blood test is performed.

It should be noted that this comprehensive examination is designed to exclude the main, most common causes of secondary arterial hypertension. In some cases,

additional, more specific tests may be required, for example, an analysis for free metanephrines in the urine if pheochromocytoma is suspected or cortisol in the daily urine if Cushing's syndrome is suspected, as well as more complex instrumental studies (ultrasound, MRI).

Regardless of the cause of arterial hypertension (primary or secondary arterial hypertension), persistent prolonged increase in blood pressure leads to irreversible changes in the vascular wall and increases the risk of developing cardiovascular diseases, including stroke and myocardial infarction. There are other risk factors for cardiovascular diseases that should be actively identified and corrected in patients with hypertension, primarily atherogenic dyslipidemia. To exclude and correct atherogenic dyslipidemia in all patients with arterial hypertension, the concentration of total cholesterol, triglycerides, cholesterol, high and low density lipoproteins (HDL-C and LDL-C) is studied. Also, in some cases, additional glucose level testing may be required to exclude concomitant diabetes mellitus.

In addition, the bibliosemantic method, as well as statistical and analytical methods were used in our scientific research.

CHAPTER 3
 FEATURES OF TREATMENT OF PATIENTS WITH ARTERIAL
 HYPERTENSION IN CERTAIN CLINICAL SITUATIONS

Our study involved 289 patients with hypertension, who were divided into groups depending on gender and age (Table 3.1., Fig. 3.1., 3.2.).

Gender and age of patients with hypertension	Number of patients	%
Women 18-39 years old	7	2.4
Women 40-59 years old	78	27.0
Women 60-90 years old	72	24.9
Men 18-39 years old	11	3.8
Men 40-59 years old	56	19.4
Men 60-90 years old	65	22.5
Total	289	100 %

Table 3.1. Distribution of patients with hypertension into groups depending on gender and age

Among the patients who took part in our scientific study there were 7 women 18-39 years old, 78 women 40-59 years old and 72 women 60-90 years old, which amounted to 157 women, as well as 11 men 18-39 years old, 56 men 40-59 years old and 65 men 60-90 years old, which amounted to 132 men.

The percentage was 54.3% women and 45.7% men.

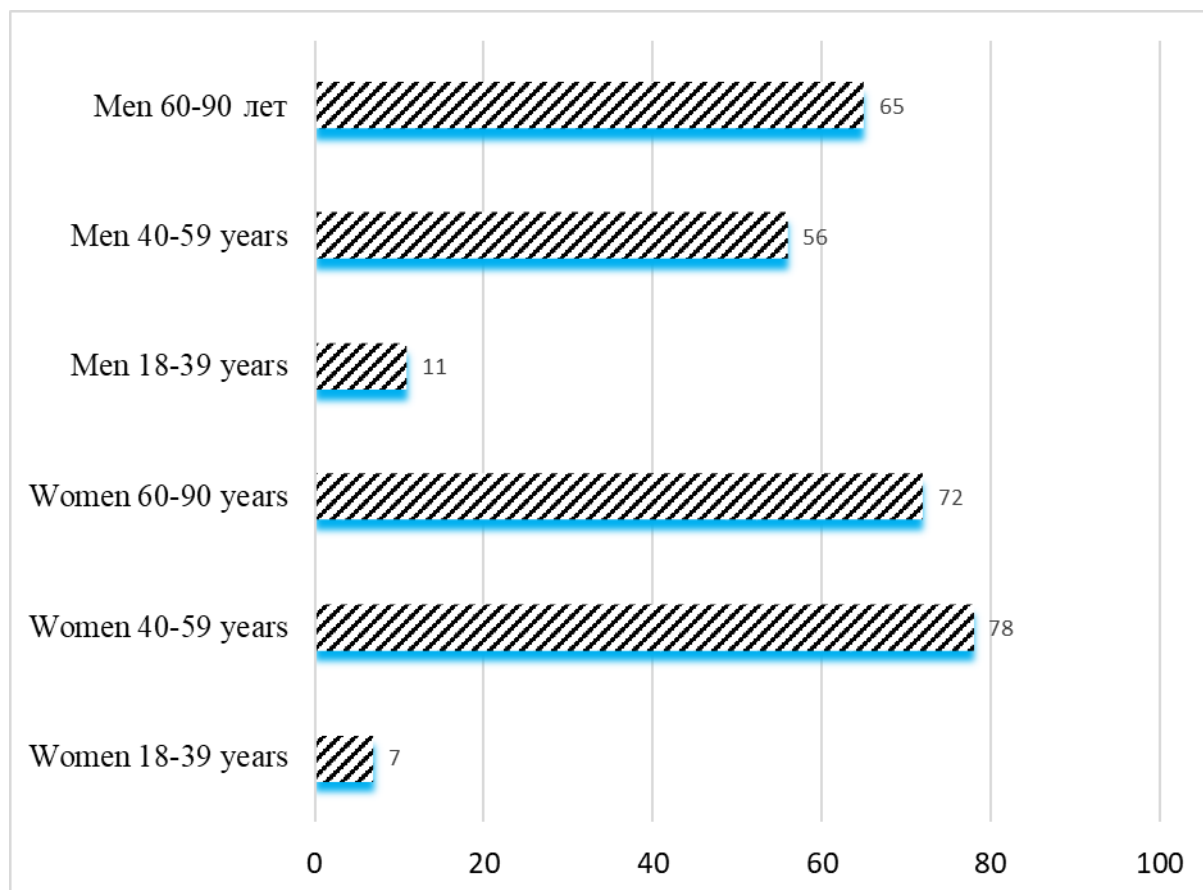


Figure 3.1. Number of patients with hypertension in groups depending on gender and age.

The basis of antihypertensive therapy for lowering blood pressure and reducing the number of cardiovascular events are 5 classes of antihypertensive drugs: ACE inhibitors, angiotensin II receptor blockers, beta-blockers, calcium channel blockers (calcium antagonists) and diuretics (thiazide - hydrochlorothiazide, and thiazide-like - chlorthalidone and indapamide).

All patients with hypertension (except low-risk patients with blood pressure <150/90 mmHg, patients ≥ 80 years of age, patients with senile asthenia syndrome), a combination of antihypertensive drugs, preferably fixed, is recommended as starting therapy to improve adherence to therapy. Preferred combinations should include renin-angiotensin-aldosterone system blockers (ACE inhibitors or angiotensin II receptor blockers) and a dihydropyridine calcium antagonist or diuretics.

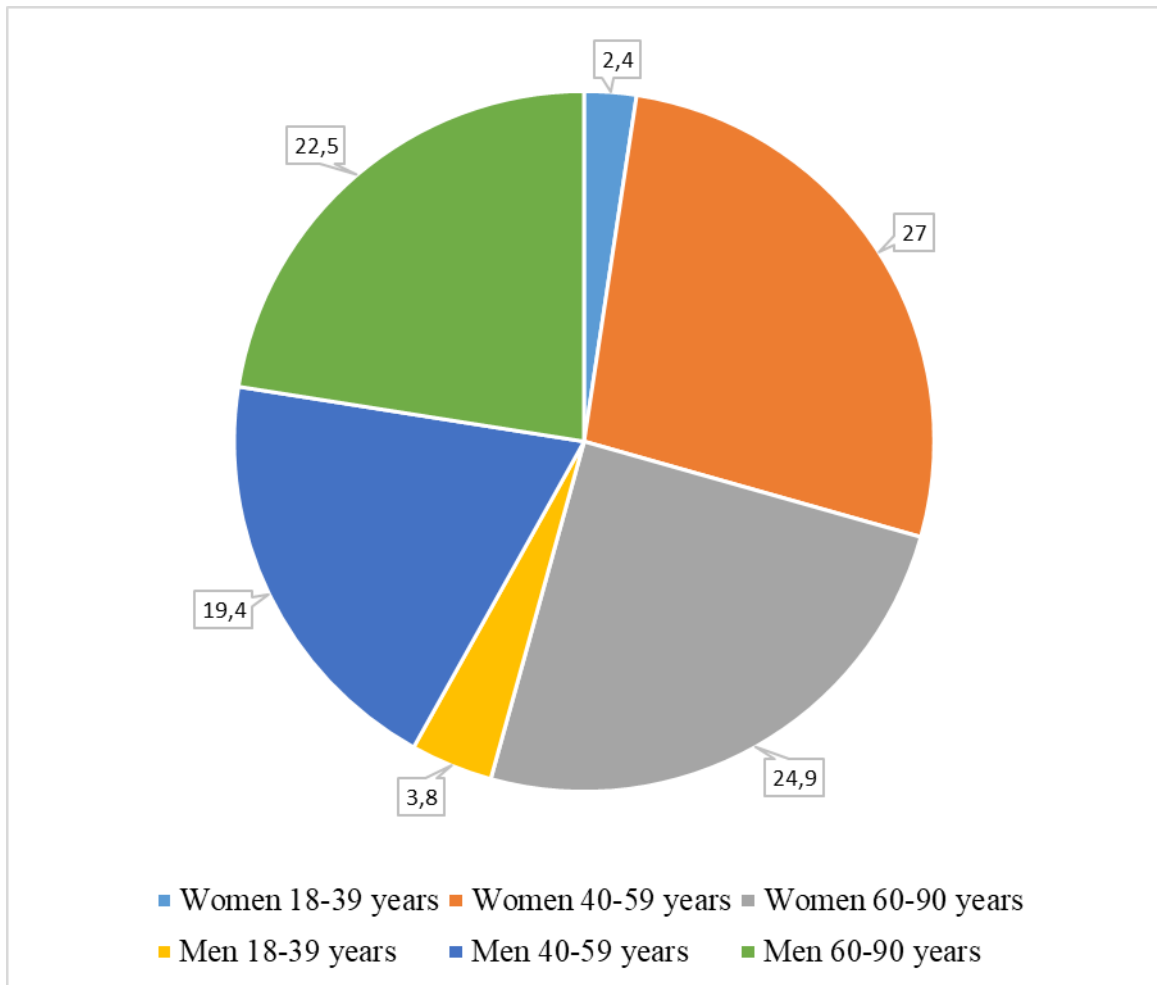


Figure 3.2. Percentage of patients with hypertension in groups depending on gender and age

We analyzed the treatment of hypertension in individual clinical situations, namely in patients with combinations of diseases:

- Arterial hypertension and diabetes mellitus
- Arterial hypertension and chronic kidney disease
- Arterial hypertension and coronary heart disease.
- Arterial hypertension, left ventricular hypertrophy and heart failure.
- Arterial hypertension and cerebrovascular disease
- Arterial hypertension in patients with lung diseases.
- Arterial hypertension during pregnancy and lactation.

Arterial hypertension and diabetes mellitus.

Patients with arterial hypertension in combination with diabetes mellitus are recommended to start antihypertensive drug therapy at blood pressure values measured in a medical institution $\geq 140/90$ mm Hg.

In patients with arterial hypertension in combination with diabetes mellitus receiving antihypertensive drug therapy, due to the proven benefits in reducing cardiovascular risk, it is recommended: as a target level, reduce SAD in patients younger than 65 years to values of 130 mmHg and lower with good tolerability, but not < 120 mmHg. In elderly patients (≥ 65 years) with diabetes mellitus, the target level of SAD is 130-139 mmHg; the target level of DAD in all patients with hypertension and diabetes mellitus is < 80 mmHg, but not < 70 mmHg.

All patients with hypertension and diabetes mellitus are recommended to start treatment with a combination of a renin-angiotensin-aldosterone system blocker with calcium antagonists (calcium channel blockers) or a thiazide/thiazide-like diuretic due to the best effect of these combinations on the frequency of achieving the target blood pressure and reducing cardiovascular risk, as well as the nephroprotective potential of renin-angiotensin blockers-aldosterone system.

The combination of diabetes mellitus and arterial hypertension deserves special attention, since both diseases significantly increase the risk of developing micro- and macrovascular lesions, including diabetic nephropathy, stroke, coronary heart disease, myocardial infarction, chronic heart failure, atherosclerosis of peripheral arteries, and contribute to an increase in cardiovascular mortality.

In the treatment of patients with arterial hypertension with diabetes mellitus, it is necessary to monitor all the risk factors available to the patient, including dyslipidemia (appointment of lipid-lowering therapy). The development of diabetic nephropathy is accompanied by a very high risk of developing cardiovascular complications, while blood pressure control and reduction of proteinuria to the lowest possible values are necessary.

Arterial hypertension and chronic kidney disease.

Patients with chronic kidney disease are recommended to start treatment (lifestyle changes and drug therapy) regardless of the presence of diabetes mellitus at a blood pressure level measured in a medical institution, $\geq 140/90$ mmHg.

Patients with diabetic and non-diabetic chronic kidney disease are recommended to reduce the SAD to values of 130-139 mmHg. due to proven benefits in reducing the risk of cardiovascular events. Individualized therapy should be prescribed depending on its tolerability and effect on kidney function and electrolyte levels.

Blockers of the renin-angiotensin-aldosterone system are recommended as a component of a therapeutic strategy in the presence of high-grade albuminuria or proteinuria, as more effective drugs to reduce the severity of albuminuria.

Hypertension is the most important factor in the development and progression of chronic kidney disease of any etiology; adequate blood pressure control slows down its development. In turn, chronic kidney disease is an important independent factor in the development and progression of cardiovascular diseases, including fatal ones. In patients receiving renal replacement therapy with hemodialysis, hypertension significantly affects survival. Accurate and correct measurement of blood pressure is extremely important for the management of such patients, however, blood pressure before a hemodialysis session may not reflect the average blood pressure level, because large fluctuations in sodium and water in the body contribute to greater variability in blood pressure. It is proved that the blood pressure measured by the method of home blood pressure monitoring is more informative than the blood pressure indicators before the hemodialysis session.

In patients with end-stage chronic kidney disease who are on dialysis, a decrease in SAD and DAD is accompanied by a decrease in the frequency of cardiovascular complications and overall mortality. Patients on hemodialysis can be prescribed all AGPS, while their doses depend on the stability of hemodynamics and the ability of a particular drug to pass through dialysis membranes. Loop diuretics are the drugs of choice among diuretics for terminal chronic kidney disease.

When using mineralocorticoid receptor antagonists, especially in combination with a renin-angiotensin-aldosterone system blocker, more careful monitoring of kidney function and potassium levels is necessary (risk of hyperkalemia).

Arterial hypertension and coronary heart disease.

Patients with hypertension in combination with coronary heart disease are recommended:

Patients younger than 65 years of age, without chronic kidney disease, receiving antihypertensive therapy, due to proven benefits in reducing the risk of cardiovascular events, it is recommended to reduce SAD to the target level of ≤ 130 mmHg with good tolerability, but not < 120 mm Hg.

In elderly patients (≥ 65 years) and / or with the presence of chronic kidney disease, it is recommended to reduce the SBP to the target values of 130-139 mmHg, to reduce the DBP to the target values of < 80 mmHg, but not < 70 mmHg.

Patients with hypertension with myocardial infarction are recommended to prescribe beta-blockers and blockers of the renin-angiotensin-aldosterone system as an integral part of therapy to reduce the risk of cardiovascular mortality.

Patients with hypertension and symptoms of angina pectoris are recommended to prescribe beta-blockers and / or calcium antagonists.

Arterial hypertension, left ventricular hypertrophy and heart failure.

Patients with hypertension in combination with heart failure (with a low or preserved ejection fraction) are recommended to prescribe antihypertensive therapy at a blood pressure level of $\geq 140/90$ mmHg due to proven benefits in reducing cardiovascular mortality.

In patients with hypertension and HF with preserved left ventricular function, when prescribing antihypertensive therapy, it is possible to use all the main drugs, since none of the drugs has demonstrated its superiority over others in terms of improving cardiovascular outcomes.

Patients with hypertension in combination with HF with a reduced ejection fraction are recommended to use ACE inhibitors or angiotensin receptor blockers, as

well as beta-blockers, diuretics and/or mineralocorticoid receptor antagonists as antihypertensive therapy, if necessary.

Arterial hypertension and cerebrovascular disease.

Patients with intracerebral hematoma and SAD <200 mmHg are not recommended to immediately reduce blood pressure to prevent complications (including hypoperfusion of the brain or an increase in the size of the lesion).

Patients with intracerebral hematoma with SAD ≥ 220 mmHg are recommended to carefully reduce blood pressure to <180 mmHg using intravenous therapy to prevent complications (including hypoperfusion of the brain or an increase in the size of the lesion).

In patients with acute ischemic stroke, routine blood pressure reduction is not recommended for the prevention of complications (including hypoperfusion of the brain)

All patients with hypertension after ischemic stroke or transient ischemic attack younger than 65 years and without CKD are recommended to reduce the SAD to the target values of 120-130 mmHg due to proven benefits in reducing cardiovascular mortality.

Antihypertensive drug therapy aimed at reducing the risk of stroke and recommended for all patients with cerebrovascular disease includes a renin-angiotensin-aldosterone system blocker in combination with calcium antagonists or a thiazide-like diuretic.

In patients with hypertension with dyscirculatory encephalopathy of II-III degree and / or transient ischemic attack /stroke in the anamnesis, hemodynamically significant stenosis of the main brachiocephalic arteries), blood pressure should not be sharply reduced, because some patients may have poor individual tolerance of lower blood pressure levels due to impaired autoregulation of cerebral vessels. In these patients, it is advisable to use a stepwise (stepwise) blood pressure reduction scheme.

Arterial hypertension in patients with lung diseases.

In patients with hypertension in combination with bronchial asthma and /or chronic obstructive pulmonary disease (COPD), in order to achieve the target blood pressure level, the appointment of beta-blockers is not recommended as a starting antihypertensive therapy, the appointment of blockers of the renin-angiotensin-aldosterone system and calcium antagonists is recommended.

The combination of hypertension with COPD and/or bronchial asthma determines the peculiarities of antihypertensive therapy.

In patients with bronchial asthma and / or COPD, the appointment of loop and thiazide diuretics requires caution, due to the high probability of hypokalemia when they are used together with β 2-agonists and especially systemic steroids.

Beta-blockers can cause the development of bronchospasm, especially non-selective ones, and therefore should not be routinely prescribed to patients with COPD and are contraindicated in patients with bronchial asthma. A number of studies conducted in a limited number of patients have shown that the use of small doses of highly selective beta-blockers does not worsen and may even slightly improve bronchial patency.

The use of calcium antagonists in patients with COPD and/or bronchial asthma is safe and even helps to reduce bronchial hyperreactivity and increase the bronchodilating effect of β 2-agonists. Thus, along with lifestyle changes (first of all, quitting smoking), the use of renin–angiotensin-aldosterone system blockers and calcium antagonists is preferable as a starting antihypertensive drug therapy. If the target blood pressure is not reached or there are concomitant diseases with appropriate indications, the addition / appointment of thiazide or thiazide-like diuretics and highly selective beta-blockers can be considered.

Patients with hypertension with bronchoobstructive pathology often use broncholytic and glucocorticosteroid drugs. Systemic and long-term use of glucocorticosteroids contributes to an increase in blood pressure. When using inhaled glucocorticosteroids, such effects are insignificant.

Arterial hypertension during pregnancy and lactation.

There are the following clinical variants of hypertension during pregnancy:

hypertension developed before pregnancy (chronic hypertension) – hypertension determined before pregnancy or manifested before 20 weeks. pregnancy and persistent >6 weeks after delivery.

Hypertension diagnosed after the 20th week of gestation and did not disappear within 6 weeks after delivery is also classified as pre-existing hypertension, but already retrospectively;

Gestational hypertension is a condition induced by pregnancy and manifested by an increase in blood pressure $\geq 140/90$ mmHg for the first time after 20 weeks, with spontaneous normalization of blood pressure within 6 weeks after delivery of blood pressure;

Preeclampsia – gestational hypertension with proteinuria >300 mg/day. or albumin / creatinine in a single portion of urine > 30 mg / mmol, in some cases with manifestations of multiple organ failure;

Chronic hypertension complicated by preeclampsia.

Pregnant women with FR, target organ damage, DM or kidney damage are recommended to have SMAD to confirm hypertension.

Women with gestational hypertension, preeclampsia, or chronic hypertension accompanied by subclinical damage to target organs are recommended to start drug therapy with SAD ≥ 140 mmHg or DAD ≥ 90 mmHg in order to reduce cardiovascular risk.

Pregnant women with increased blood pressure without signs of target organ damage, preeclampsia and associated clinical condition in order to reduce cardiovascular risk, initiation of drug therapy is recommended for SAD ≥ 150 mmHg or DAD ≥ 95 mmHg.

The purpose of treatment of pregnant women with hypertension is to prevent the development of complications due to high levels of Blood pressure, to ensure the preservation of pregnancy, normal fetal development and successful childbirth. The

target blood pressure level for pregnant women is $<140/90$ mmHg. Episodes of hypotension should not be allowed to develop, so as not to worsen placental blood flow.

Pregnant women with SAD ≥ 170 and DAD ≥ 110 mmHg are recommended to be urgently hospitalized and regard this condition as GC.

The main rule in the treatment of GC in pregnant women is a controlled decrease in SAD to <160 and DBP to <105 mmHg. For oral therapy, methyldopa or delayed-release nifedipine should be used. For the treatment of preeclampsia with pulmonary edema, nitroglycerin is the drug of choice, the duration of its use should not be > 4 hours, due to the negative effect on the fetus and the risk of developing cerebral edema in the mother. The use of diuretics is not indicated, because with preeclampsia, the volume of circulating blood decreases. To prevent eclampsia and treat seizures, it is recommended to inject magnesium sulfate.

Women with a high risk of preeclampsia are recommended to prescribe small doses (150 mg) of aspirin from the 12th week in order to prevent it. pregnancy and up to the 36th week, provided there is a low risk of gastrointestinal bleeding.

CHAPTER 4
URGENT CONDITIONS
AGAINST THE BACKGROUND OF A PRONOUNCED INCREASE IN
BLOOD PRESSURE

Emergency conditions include lesions of target organs (brain, cardiovascular system and kidneys) against the background of a pronounced increase in blood pressure. Diagnosis is made by measuring blood pressure, performing an ECG, urinalysis, creatinine level and urea nitrogen concentration in blood serum. Treatment consists in immediate reduction of blood pressure by intravenous administration of drugs (for example, clevidipine, phenoldopam, nitroglycerin, nitroprusside, nicardipine, labetalol, esmolol, hydralazine).

Target organ damage includes hypertensive encephalopathy, pre-eclampsia and eclampsia, acute left ventricular heart failure with pulmonary edema, myocardial ischemia, acute aortic dissection and acute renal failure. The damage progresses extremely quickly and can lead to death.

Hypertensive encephalopathy can lead to impaired autoregulation of cerebral vessels. Normally, with an increase in blood pressure, the vessels of the brain narrow to maintain constant perfusion. When the average blood pressure (SAD) rises above 160 mm Hg (or less – for patients without hypertension, who have a sharp increase in blood pressure), the narrowed cerebral vessels begin to expand. As a result, this leads to a strong increase in pressure in the capillary bed with transudation and exudation of plasma components into brain tissue, which causes the development of cerebral edema, including edema of the optic disc.

Emergency condition on the background of increased blood pressure	The number of patients with an emergency condition on the background of increased blood pressure	%
Hypertensive encephalopathy	9	3,1
Preeclampsia and eclampsia	4	1,4
Acute left ventricular heart failure with pulmonary edema	4	1,4
Myocardial ischemia	12	4,1
Acute aortic dissection	3	1,0
Acute renal failure	9	3,1
Total	41	14,2
A total of patients with elevated blood pressure who participated in our study	289	100

Table 4.1. Emergency conditions on the background of a pronounced increase in blood pressure.

When analyzing the frequency of emergency conditions against the background of a pronounced increase in blood pressure in patients who participated in our study, it was revealed that 9 patients (3.1%) with hypertensive encephalopathy manifested, 4 patients (1.4%) showed pre-eclampsia and eclampsia, 4 patients (1.4%) showed acute left ventricular heart failure with pulmonary edema, myocardial ischemia in 12 patients (1.4%), acute aortic dissection manifested in 3 patients (1.0%), acute renal failure – in 9 patients (3.1%), which totaled 41 patients (14.2%) of the total number of patients with elevated blood pressure who participated in our study (289 patients).

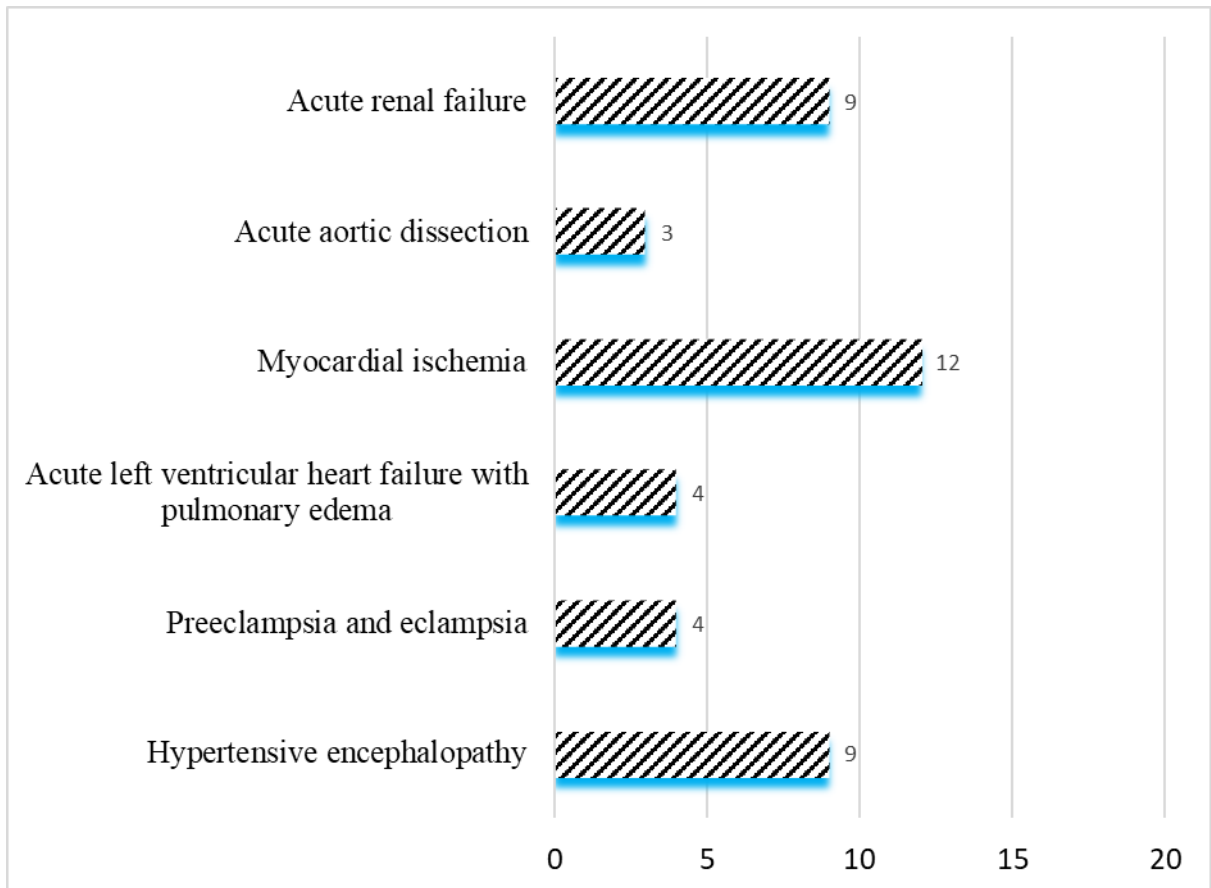


Figure 4.1. The number of patients with emergency conditions that occurred against the background of a pronounced increase in blood pressure

Although a large number of patients with strokes and intracranial hemorrhages have elevated blood pressure figures, often hypertension is not the cause, but the consequence of this. In such cases, a rapid decrease in blood pressure may be impractical and even dangerous.

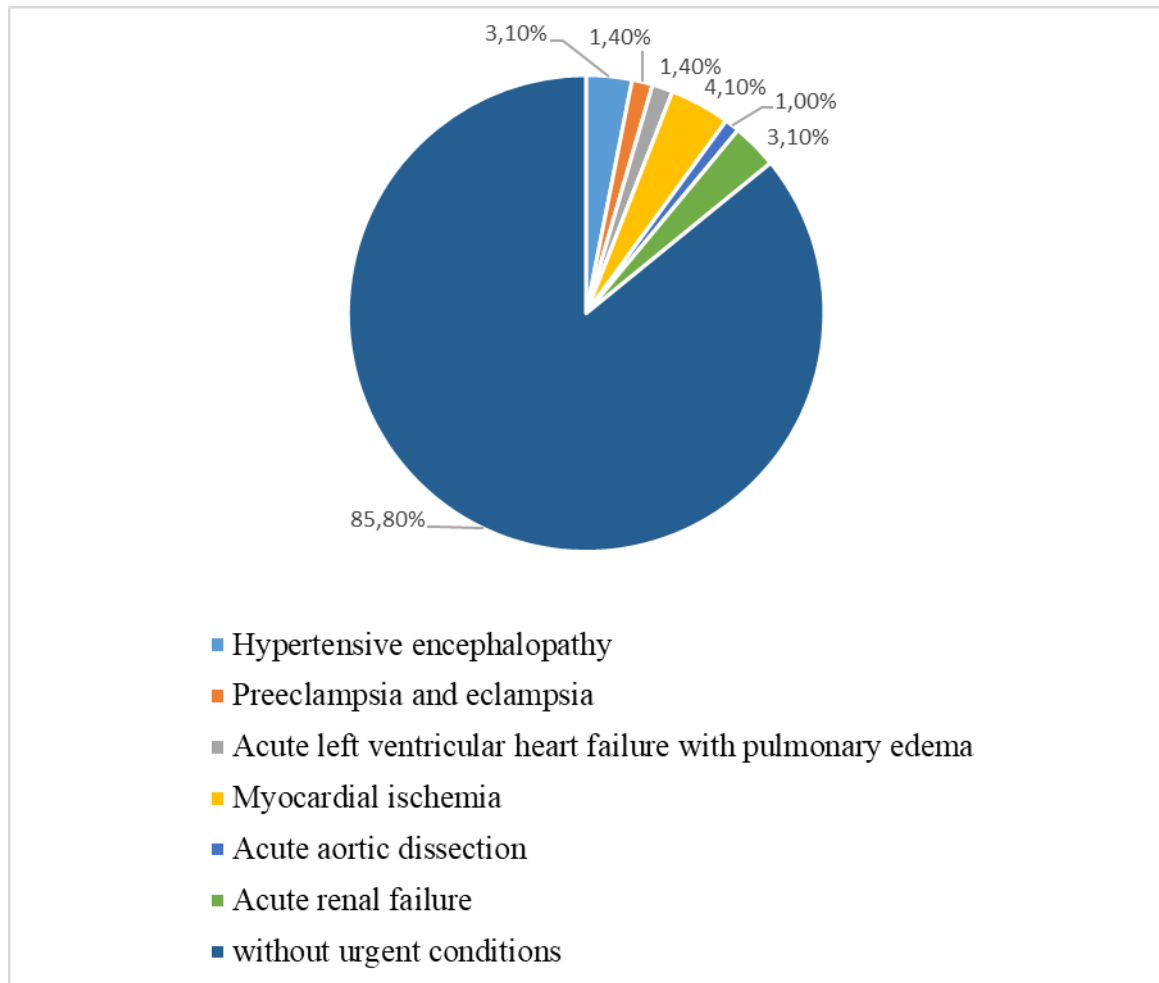


Figure 4.2. Percentage of patients with emergency conditions that occurred against the background of a pronounced increase in blood pressure, and patients without emergency conditions

Complications requiring emergency intervention.

Very high blood pressure (for example, diastolic blood pressure $> 120-130$ mmHg) without damage to the target organs (with the exception of stage 1-3 retinopathy) can be regarded as an emergency condition. Such high blood pressure indicators often cause alarm among doctors, but they are rarely accompanied by complications, so they do not require an emergency reduction. In these patients, therapy should be started with a combination of 2 antihypertensive drugs and subsequently monitored on an outpatient basis. Very high blood pressure without organ

damage is usually found in patients with a high degree of anxiety or in those who have had very poor sleep quality for several weeks.

Clinical manifestations.

Blood pressure is elevated, often to a significant extent (diastolic pressure > 120 mmHg). Symptoms from the central nervous system (CNS) are characterized by rapid changes and include confusion, transient loss of visual fields, hemiparesis, hemiparasthesia, loss of consciousness. Cardiovascular symptoms include chest pain and shortness of breath. Kidney involvement may be asymptomatic, but severe azotemia leads to nausea and loss of consciousness.

Physical examination should be directed to the target organs: neurological examination, fundus examination, examination of the cardiovascular system. Isolated focal deficits indicate a stroke. General cerebral disorders (confusion, deafness, coma), accompanied by focal symptoms or without it, should be interpreted as encephalopathy. Severe retinopathy (sclerosis, focal retinal changes, narrowing of arterioles, hemorrhages, edema of the optic nerve) often accompanies hypertensive encephalopathy; retinopathy of various degrees is often present in many others hypertensive crises. Swelling of the jugular veins, wet wheezing in the lungs, the appearance of the III tone indicates the beginning of pulmonary edema. The asymmetry of the pulse in the upper extremities suggests aortic dissection.

Diagnostics.

Very high blood pressure.

Detection of target organ damage: ECG, urine analysis, creatinine content and concentration of urea nitrogen in the blood (AMC), CT of the brain in the presence of neurological symptoms.

The examination usually includes an ECG, a general urinalysis, determination of blood urea nitrogen and creatinine levels.

Patients with neurological symptoms require a CT scan of the head for intracranial bleeding, edema or heart attack.

In patients with chest pain or shortness of breath, chest radiography is necessary.

With the help of an ECG, violations are detected, suspected damage to the target organs include signs of left ventricular hypertrophy or acute ischemia.

Typical deviations from the norm in the general analysis of urine, when the kidneys are involved in the pathological process, are the presence of erythrocytes, erythrocyte cylinders and proteinuria.

The diagnosis is based on a combination of very high blood pressure with damage to the target organs.

Treatment.

You should be hospitalized in the intensive care unit.

Short-term drugs for intravenous administration: nitrates, phenoldopam, nicardipine or labetalol.

Goal: reduction of average blood pressure by 20-25% in 1-2 hours.

Hypertensive crises are treated in the intensive care unit; blood pressure is progressively (but not sharply) reduced using titrated short-acting drugs for intravenous administration. The choice of the drug, dose, and rate of administration depends on the affected target organ, but on average it is necessary to reduce blood pressure by 20-25% during the first hour, followed by titration of the dose, depending on the symptoms. Achieving normal blood pressure in the shortest possible time is not advisable. The main first-line drugs are nitroprusside, phenoldopam, nicardipine and labetalol (see table Parenteral drugs in the treatment of complicated hypertensive crisis). Nitroglycerin in monotherapy is less effective.

Oral medications are not prescribed due to the variability of the occurrence of crises and the difficulty of dose selection. Although short-acting nifedipine when taken orally quickly lowers blood pressure, however, it can provoke the development of acute cardiovascular and cerebral events (sometimes fatal), and therefore it is not recommended.

Clevidipine is an ultrashort drug (within 1-2 minutes), a third-generation calcium channel blocker that reduces peripheral vascular resistance without affecting venous vascular tone and cardiac filling pressure. Clevidipine is rapidly hydrolyzed by blood

esterases and, thus, its metabolism does not depend on kidney or liver function. It proved to be more effective and safe in the control of perioperative hypertension and hypertensive crises, its use compared with nitroprusside was associated with lower mortality.

The initial dose of clevidipine is from 1 to 2 mg / hour, with a doubling of the dose every 90 seconds until the required blood pressure level is reached, after which the dose is increased less than twice every 5-10 minutes. Clevidipine, therefore, may be more preferable than nitroprusside for most hypertensive crises, although it should be used with caution in acute heart failure with a reduced ejection fraction, since its use can cause negative inotropic effects. If clevidipine is not available, then phenoldopam, nitroglycerin or nicardipine are a good alternative.

Nitroprusside causes dilation of veins and arteries, reducing preload and postload, so this drug is best suited for patients with hypertension on the background of heart failure. It is also used for hypertensive encephalopathy and, in combination with beta blockers, for aortic dissection. The starting dose is 0.25-1.0 mcg / kg / minute with a titration from 0.5 mcg / kg / minute to a maximum of 8-10 mcg / kg / minute; the maximum dose is administered for less than 10 minutes to reduce the risk of cyanide intoxication. The drug is rapidly broken down into cyanide and nitric oxide (the active component). Cyanide is detoxified into thiocyanate. However, administration of > 2 micrograms/ kg/minute can lead to the accumulation of cyanides with toxicity to the central nervous system and the heart. Symptoms include anxiety, seizures, unstable heart function, and metabolic acidosis with an anion gap.

Prolonged administration of nitroprusside (> 1 week or – in patients with renal insufficiency - 3-6 days) leads to the accumulation of thiocyanate, which is manifested by lethargy, tremor, abdominal pain, vomiting. Other undesirable effects include a transient rise in hair follicles (goose bumps) if blood pressure decreases too quickly. The thiocyanate level should be monitored daily after 3 consecutive days of therapy; if the plasma thiocyanate level is > 12 mg/dl (> 2 mmol/L), therapy should be discontinued. Since nitroprusside is destroyed by ultraviolet radiation, the container

with the drug and the intravenous infusion tubes should be wrapped with an opaque material. Given the data on the increase in mortality when using nitroprusside compared to clevidipine, nitroglycerin, nicardipine, it should not be used when other alternatives are available.

Phenoldopam is an agonist of peripheral dopamine-1 receptors, which leads to dilation of systemic and renal vessels and natriuresis. The rapid onset of action and short half-life make it a good alternative to nitroprusside. Moreover, the drug does not penetrate the blood-brain barrier. The initial dose is 0.1 mcg / kg / minute intravenously with titration from 0.1 mcg / kg every 15 minutes to a maximum dose of 1.6 mcg / kg / minute.

Nitroglycerin is a vasodilator that has a stronger effect on veins than on arterioles. It can be used to control hypertension during and after coronary artery surgery, acute myocardial infarction, unstable angina and acute pulmonary edema. Administered intravenously, nitroglycerin is more preferable than nitroprusside in patients with severe damage to the coronary bed due to increased coronary blood flow by the former and its weakening in ischemic areas by the latter. The starting dose is 10-20 mcg / minute with a titration of 10 mcg / minute every 5 minutes until the maximum antihypertensive effect.

For long-term blood pressure control, the addition of other antihypertensive drugs is required. The most common side effect is headache (2%), the rest are tachycardia, nausea, vomiting, anxiety, fear of death, muscle cramps.

Nicardipine is a dihydropyridine calcium channel blocker, which has a lower negative inotropic effect than nifedipine, and acts primarily as a vasodilator. It is most often used for postoperative blood pressure monitoring and during pregnancy. The dose of 5 mg / hour intravenously is increased every 15 minutes to a maximum of 15 mg / hour, which can cause hyperemia, headache and tachycardia. This can cause hyperemia, headache and tachycardia; it can reduce the glomerular filtration rate (GFR) in patients with renal insufficiency.

Labetalol is a beta-blocker with a moderate alpha-1-blocking effect, which allows to provoke vasodilation without reflex tachycardia. It can be prescribed both for permanent infusion and episodically bolus, which does not lead to the development of significant hypotension. Labetalol is used during pregnancy, in the case of intracranial disorders to control blood pressure and after myocardial infarction. Infusion of 0.5–2 mg / minute with gradual titration to maximum doses of 4-5 mg / minute. Bolus – 20 mg intravenously, followed by 40 mg every 10 minutes, then 80 mg (up to 3 times) until the maximum total dose of 300 mg is reached. Undesirable effects are minimal, however, due to the beta-blocking effect, labetalol should not be prescribed for hypertensive crisis in patients with bronchial asthma. In low doses, it can be used for the treatment of left ventricular heart failure, in parallel with nitrate therapy.

Hypertensive crisis is arterial hypertension that causes damage to target organs; it requires intravenous therapy and hospitalization.

Target organ damage includes hypertensive encephalopathy, pre-eclampsia and eclampsia, acute left ventricular heart failure with pulmonary edema, myocardial ischemia, acute aortic dissection and acute renal failure.

It is necessary to do an ECG, a general urinalysis, determine the levels of serum urea nitrogen and creatinine, CT of the head for patients with neurological symptoms or signs.

Reduce average blood pressure by about 20-25% during the first hour after intravenous administration of short-acting titrated drugs such as clevidipine, nitroglycerin, phenoldopam, nicardipine or labetalol.

Medical staff should remember that there is no need to quickly reduce blood pressure to "normal numbers" (especially in acute stroke). Stroke patients require a special approach, because excessive and/or rapid decrease in blood pressure can lead to an increase in cerebral ischemia.

In most other cases, doctors are recommended to ensure a rapid, but no more than 25% of the initial values, reduction in blood pressure for the first 2 hours from the moment of admission to the hospital.

CHAPTER 5

MEDICAL REHABILITATION, DISPENSARY SUPERVISION, PRIMARY AND SECONDARY PREVENTION OF ARTERIAL HYPERTENSION

Medical rehabilitation, medical indications and contraindications to the use of rehabilitation methods.

For all patients with hypertension, it is recommended to develop an individual rehabilitation plan, which includes recommendations for achieving the target BP, self-monitoring of BP, increasing adherence to treatment, nutrition, physical activity, weight control.

In order to reduce the risk of cardiovascular complications, all patients with hypertension are recommended at least 150 minutes (2 hours 30 minutes) per week of moderate-intensity aerobic physical activity or 75 minutes (1 hour 15 minutes) per week of high-intensity aerobic physical activity.

Moderate physical activity is a load that can be sustained for 1 hour, and intense physical activity is one in which fatigue appears after 30 minutes. During physical exertion, blood pressure monitoring is mandatory.

Prevention and dispensary supervision, medical indications and contraindications to the use of prevention methods.

Dynamic monitoring is an extremely important component of medical care for patients with hypertension, whose tasks are: maintaining target blood pressure levels, monitoring the implementation of medical recommendations for correcting risk factors, monitoring compliance with the antihypertensive therapy regimen, assessing the condition of target organs.

With a stable course of hypertension, home monitoring of blood pressure can be an acceptable alternative to visits to a medical institution.

All recommendations given to the patient should be clear, clear and correspond to his intellectual level.

In order to ensure the patient's conscious participation in the therapeutic and preventive process and to increase the effectiveness of treatment, it is advisable for a number of patients for whom oral recommendations are not enough to duplicate them in writing.

All patients with high blood pressure, which is still within the normal range (130-139/85-89 mmHg), are recommended to change their lifestyle.

Hypertension, like any chronic progressive disease, is easier to prevent than to treat. Therefore, the prevention of hypertension, especially for people with burdened heredity, is a task of the first necessity.

First of all, it is worth thinking about the prevention of hypertension for everyone whose blood pressure is within the high or borderline norm, especially for young people and adolescents.

Prevention of arterial hypertension can be primary and secondary.

Primary refers to the prevention of the occurrence of the disease. These methods of prevention should be followed by healthy people who have a high risk of hypertension (heredity, work). But not only they, everyone should live in accordance with the principles of primary prevention of hypertension, because this disease often overtakes at the most unexpected moment even those who do not have unfavorable heredity and other risk factors.

Primary prevention of hypertension includes:

- Normalization of the function of the central nervous system (prevention of stress).
- A clear daily routine (constant time of getting up and going to bed).
- Outdoor exercises and physical therapy (long walks in the fresh air, cycling, moderate work in the garden).
- Daily loads in the gym and at home.
- Normalization of sleep (sleep lasting up to 8 hours).
- Rational nutrition. Carefully count the calories consumed with food, do not allow excessive fat consumption. Fats can be consumed no more than 50-60 grams per

day, and 2/3 of them should be vegetable fats: corn, sunflower oil. Limit foods containing large amounts of animal fats – whole milk, butter, sour cream. The diet should contain a sufficient amount of proteins: low-fat varieties of fish, poultry, skimmed milk, cottage cheese, kefir, etc. It is necessary to limit the intake of easily digestible carbohydrates: sugar, honey, pastry products, chocolate, semolina, rice cereals.

- Weight loss (in case of obesity). Without weight loss, it is not necessary to talk about the prevention of hypertension. You can not try to lose weight dramatically, you can reduce body weight by 5-10% per month.

- Quitting smoking!!!
- Reducing the use of table salt (use no more than 6 grams per day).
- Consumption of foods with a high content of potassium, calcium and magnesium salts (low-fat cottage cheese, parsley, beans, prunes, beets, baked potatoes, dried apricots, pitted raisins.)
- Restriction of alcohol consumption.

Secondary prevention is carried out in patients who have arterial hypertension as a diagnosis. Its purpose is to prevent the occurrence of complications. At the same time, this type of prevention includes two components: non-drug treatment of hypertension and antihypertensive (drug) therapy. Non-drug treatment, in principle, corresponds to primary prevention, only with stricter requirements. If each individual is unable to change heredity and the environment, then the lifestyle and nutrition are quite. Drug therapy - medications prescribed by a doctor that purposefully act on a high level of pressure, reducing it. Patients with arterial hypertension should strictly adhere to the doctor's recommendations and take medications as prescribed, thereby preventing the risk of complications.

The prevention of hypertension can include systematic monitoring of blood pressure levels in the morning and evening. Relentless adherence to the recommendations of the nurse and the attending physician, timely access to him in case of condition deterioration.

CONCLUSION

1. The epidemiology, etiology and pathogenesis of arterial hypertension have been studied.
2. The classification and clinic of arterial hypertension have been studied.
3. The features of the treatment of patients with arterial hypertension in certain clinical situations have been investigated.
4. Urgent conditions were investigated against the background of a pronounced increase in blood pressure.
5. The features of medical rehabilitation, dispensary supervision, primary and secondary prevention of hypertension have been studied.

LIST OF LITERATURE

1. Aburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ*. 2013; 346:f1326.
2. Albasri A, O'Sullivan JW, Roberts NW, et al. A comparison of blood pressure in community pharmacies with ambulatory, home and general practitioner office readings: systematic review and meta-analysis. *J Hypertens*. 2017 Oct;35(10):1919-1928. doi:10.1097/HJH.0000000000001443.
3. Bacharova L, Schocken D, Estes EH, Strauss D. The role of ECG in the diagnosis of left ventricular hypertrophy. *Curr Cardiol Rev*. 2014; 10: 257-61.
4. Berrington de Gonzalez A, Hartge P, Cerhan JR, et al. Body-mass index and mortality among 1.46 million white adults. *N Engl J Med*. 2010 Dec 2;363(23):2211-9. doi:10.1056/NEJMoa1000367.
5. Boekholdt SM, Arsenault BJ, Mora S, et al. Association of LDL cholesterol, non-HDL cholesterol, and apolipoprotein B levels with risk of cardiovascular events among patients treated with statins: a meta-analysis. *JAMA*. 2012 Mar 28;307(12):1302-9. doi:10.1001/jama.2012.366.
6. Brown DW, Giles WH, Greenlund KJ. Blood pressure parameters and risk of fatal stroke, NHANES II mortality study. *Am J Hypertens*. 2007; 20:338-41.
7. Clark CE, Taylor RS, Shore AC, et al. Association of a difference in systolic blood pressure between arms with vascular disease and mortality: a systematic review and meta-analysis. *Lancet*. 2012; 379:905-14.
8. Cosentino F, Grant P, Aboyans V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: The Task Force for diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD). *Eur Heart J*. 2020 Jan 7;41(2):255-323. doi:10.1093/eurheartj/ehz486.

9. Earley A, Miskulin D, Lamb EJ, et al. Estimating equations for glomerular filtration rate in the era of creatinine standardization: a systematic review. *Ann Intern Med.* 2012; 156:785-95.
10. Egan BM, Bandyopadhyay D, Shaftman SR, et al. Initial monotherapy and combination therapy and hypertension control the first year. *Hypertension* 2012;59: 1124-31.
11. Ehret GB, Caulfield MJ. Genes for blood pressure: an opportunity to understand hypertension. *Eur Heart J.* 2013; 34:951-61.
12. Emerging Risk Factors Collaboration, Sarwar N, Gao P, Seshasai SR, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet.* 2010 Jun 26;375(9733):2215-22. doi:10.1016/S0140-6736(10)60484-9.
13. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet.* 2016; 387:957-67.
14. Fagard RH, Celis H, Thijs L, et al. Daytime and night-time blood pressure as predictors of death and cause-specific cardiovascular events in hypertension. *Hypertension.* 2008; 51:55-61.
15. Fagard RH, Cornelissen VA. Incidence of cardiovascular events in white-coat, masked and sustained hypertension vs. true normotension: a meta-analysis. *J Hypertens.* 2007; 25:2193-219.
16. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *JAMA.* 2013; 309:71-82.
17. Franklin SS, Lopez VA, Wong ND, et al. Single versus combined blood pressure components and risk for cardiovascular disease: the Framingham Heart Study. *Circulation.* 2009; 119:243-50.
18. Gay HC, Rao SG, Vaccarino V, Ali MK. Effects of different dietary interventions on blood pressure: systematic review and meta-analysis of randomized

controlled trials. *Hypertension*. 2016 Apr;67(4):733-9. doi:10.1161/HYPERTENSIONAHA.115.06853.

19. Gottesman RF, Albert MS, Alonso A, et al. Associations between midlife vascular risk factors and 25-year incident dementia in the Atherosclerosis Risk in Communities (ARIC) cohort. *JAMA. Neurol*. 2017; 74:1246-54.

20. Graudal NA, Hubeck-Graudal T, Jurgens G. Effects of low-sodium diet vs. high-sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride (Cochrane Review). *Am J Hypertens*. 2012; 25:1-15.

21. Grayson PC, Kim SY, LaValley M, Choi HK. Hyperuricemia and incident hypertension: a systematic review and meta-analysis. *Arthritis Care Res (Hoboken)*. 2011 Jan;63(1):102-10. doi:10.1002/acr.20344.

22. Guo X, Zou L, Zhang X, et al. Prehypertension: a meta-analysis of the epidemiology, risk factors, and predictors of progression. *Tex Heart Inst J*. 2011;38(6):643-52.

23. Himmelfarb CR, Commodore-Mensah Y, Hill MN. Expanding the Role of Nurses to Improve Hypertension Care and Control Globally. *Ann Glob Health*. 2016 Mar-Apr;82(2):243-53. doi: 10.1016/j.aogh.2016.02.003. PMID: 27372529.

24. Izzo R, de Simone G, Trimarco V, et al. Hypertensive target organ damage predicts incident diabetes mellitus. *Eur Heart J*. 2013 Nov;34(44):3419-26. doi:10.1093/eurheartj/eh281.

25. Kearney PM, Whelton M, Reynolds K, et al. Global burden of hypertension: analysis of worldwide data. *Lancet*. 2005; 365:217-23.

26. Kollias A, Ntineri A, Stergiou GS. Association of night-time home blood pressure with night-time ambulatory blood pressure and target-organ damage: a systematic review and meta-analysis. *J Hypertens*. 2017 Mar;35(3):442-52. doi: 10.1097/HJH.0000000000001189.

27. Lehtonen AO, Puukka P, Varis J, et al. Prevalence and prognosis of ECG abnormalities in normotensive and hypertensive individuals. *J Hypertens*. 2016; 34:959-66.

28. Leitzmann MF, Park Y, Blair A, et al. Physical activity recommendations and decreased risk of mortality. *Arch Intern Med.* 2007 Dec 10;167(22):2453-60.
29. Linneberg A, Jacobsen RK, Skaaby T, et al. Effect of smoking on blood pressure and resting heart rate: a mendelian randomization meta-analysis in the CARTA Consortium. *Circ Cardiovasc Genet.* 2015 Dec;8(6):832-41. doi:10.1161/CIRCGENETICS.115.001225.
30. Lip GYH, Coca A, Kahan T, et al. Hypertension and cardiac arrhythmias: executive summary of a consensus document from the European Heart Rhythm Association (EHRA) and ESC Council on Hypertension, endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulacion Cardiaca y Electrofisiologia (SOLEACE). *Eur Heart J Cardiovasc Pharmacother.* 2017; 3:235-50.
31. MacDonald TM, Williams B, Webb DJ, et al. British Hypertension Society Programme of Prevention And Treatment of Hypertension With Algorithm-based Therapy (PATHWAY). Combination therapy is superior to sequential monotherapy for the initial treatment of hypertension: a double-blind randomized controlled trial. *J Am Heart Assoc.* 2017; 6:e006986.
32. Mahmoodi BK, Matsushita K, Woodward M, et al. Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without hypertension: a meta-analysis. *Lancet.* 2012 Nov 10;380(9854):1649-61. doi:10.1016/S0140-6736(12)61272-0.
33. Mancia G, Facchetti R, Bombelli M, et al. Long-term risk of mortality associated with selective and combined elevation in office, home and ambulatory blood pressure. *Hypertension.* 2006; 47:846-53.
34. Matsushita K, Coresh J, Sang Y, et al. Kidney measures beyond traditional risk factors for cardiovascular prediction: A collaborative meta-analysis. *Lancet Diabetes Endocrinol.* 2015 Jul;3(7):514-25. doi:10.1016/S2213-8587(15)00040-6.
35. Matsushita K, Mahmoodi BK, Woodward M, et al. Comparison of risk prediction using the CKD–EPI equation and the MDRD study equation for estimated

glomerular filtration rate. *JAMA*. 2012 May 9;307(18):1941-51. doi:10.1001/jama.2012.3954.

36. Matsuzaki M, Ogihara T, Umemoto S, et al. Combination Therapy of Hypertension to Prevent Cardiovascular Events Trial Group. Prevention of cardiovascular events with calcium channel blocker-based combination therapies in patients with hypertension: a randomized controlled trial. *J Hypertens*. 2011; 29:1649-59.

37. Okin PM, Devereux RB, Jern S, et al. LIFE Study Investigators. Regression of electrocardiographic left ventricular hypertrophy during antihypertensive treatment and the prediction of major cardiovascular events. *JAMA* 2004; 292:2343-9.

38. Palmer TM, Nordestgaard BG, Benn M, et al. Association of plasma uric acid with ischaemic heart disease and blood pressure: mendelian randomisation analysis of two large cohorts. *BMJ*. 2013 Jul 18;347:f4262. doi:10.1136/bmj.f4262.

39. Parati G, Stergiou G, O'Brien E, et al, European Society of Hypertension Working Group on Blood Pressure Monitoring and Cardiovascular Variability. European Society of Hypertension practice guidelines for ambulatory blood pressure monitoring. *J Hypertens*. 2014; 32:1359-66.

40. Perrone-Filardi P, Coca A, Galderisi M, et al. Non-invasive cardiovascular imaging for evaluating subclinical target organ damage in hypertensive patients: a consensus paper from the European Association of Cardiovascular Imaging (EACVI), the European Society of Cardiology Council on Hypertension, and the European Society of Hypertension (ESH). *Eur Heart J Cardiovasc Imaging*. 2017; 18:945-60.

41. Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet*. 2014 May 31;383(9932):1899-911. doi:10.1016/S0140-6736(14)60685-1.

42. Reino-Gonzalez S, Pita-Fernández S, Seoane-Pillado T, et al. How in-office and ambulatory BP monitoring compare: A systematic review and meta-analysis. *J Fam Pract*. 2017 Jan; 66(1):E5-E12.

43. Rimoldi SF, Scherrer U, Messerli FH. Secondary arterial hypertension: when, who, and how to screen? *Eur Heart J*. 2014; 35:1245-54.
44. Rossi A, Dikareva A, Bacon SL, Daskalopoulou SS. The impact of physical activity on mortality in patients with high blood pressure: a systematic review. *J Hypertens*. 2012 Jul;30(7):1277-88. doi:10.1097/HJH.0b013e3283544669.
45. Rovio SP, Pahkala K, Nevalainen J, et al. Cardiovascular risk factors from childhood and midlife cognitive performance: the Young Finns study. *J Am Coll Cardiol*. 2017; 69:2279-89.
46. Salles GF, Reboldi G, Fagard RH, et al. Prognostic effect of the nocturnal blood pressure fall in hypertensive patients: the Ambulatory Blood pressure Collaboration in patients with Hypertension (ABC-H) meta-analysis. *Hypertension*. 2016; 67:693-700.
47. Schillaci G, Battista F, Pucci G. A review of the role of electrocardiography in the diagnosis of left ventricular hypertrophy in hypertension. *Journal of electrocardiology*. 2012;45(6):617-23.
48. Sega R, Facchetti R, Bombelli M, et al. Prognostic value of ambulatory and home blood pressures compared with office blood pressure in the general population: follow-up results from the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study. *Circulation*. 2005; 111:1777-83.
49. Sehestedt T, Jeppesen J, Hansen TW, et al. Risk prediction is improved by adding markers of subclinical organ damage to SCORE. *Eur Heart J*. 2010; 31:883-91.
50. Shi Y, Zhou W, Liu X, et al. Resting heart rate and the risk of hypertension and heart failure: a dose-response meta-analysis of prospective studies. *J Hypertens*. 2018 May;36(5):995- 1004. doi:10.1097/HJH.0000000000001627.
51. Taylor RS, Ashton KE, Moxham T, et al. Reduced dietary salt for the prevention of cardiovascular disease: a meta-analysis of randomized controlled trials (Cochrane review). *Am J Hypertens*. 2011; 24:843-53.

52. Tucker KL, Sheppard JP, Stevens R, et al. Self-monitoring of blood pressure in hypertension: a systematic review and individual patient data meta-analysis. *PLoS Med.* 2017; 14:e1002389.
53. Van Der Velde M, Matsushita K, Coresh J, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts. *Kidney Int.* 2011 Jun;79(12):1341-52. doi:10.1038/ki.2010.536.
54. Vanezis AP, Bhopal R. Validity of electrocardiographic classification of left ventricular hypertrophy across adult ethnic groups with echocardiography as a standard. *Journal of Electrocardiology.* 2008;41(5):404-12.
55. Vishram JK, Borglykke A, Andreassen AH, et al, MORGAM Project. Impact of age on the importance of systolic and diastolic blood pressures for stroke risk: the MONica, Risk, Genetics, Archiving, and Monograph (MORGAM) project. *Hypertension.* 2012; 60:1117-23.
56. Vlachopoulos C, Aznaouridis K, Terentes-Printzios D, et al. Prediction of Cardiovascular Events and All-Cause Mortality With Brachial-Ankle Elasticity Index: A Systematic Review and Meta-Analysis. *Hypertension.* 2012; 60(2):556-62.
57. Volpe M, Battistoni A, Tocci G, et al. Cardiovascular risk assessment beyond systemic coronary risk estimation: a role for organ damage markers. *J Hypertens.* 2012; 30:1056-64.
58. Wang J, Qin T, Chen J, et al. Hyperuricemia and risk of incident hypertension: a systematic review and meta-analysis of observational studies. *PLoS One.* 2014 Dec 1; 9(12):e114259. doi:10.1371/journal.pone.0114259.
59. Ward AM, Takahashi O, Stevens R, Heneghan C. Home measurement of blood pressure and cardiovascular disease: systematic review and meta-analysis of prospective studies. *J Hypertens.* 2012; 30:449-56.
60. Ward AM, Takahashi O, Stevens R, Heneghan C. Home measurement of blood pressure and cardiovascular disease: systematic review and meta-analysis of prospective studies. *J Hypertens.* 2012; 30:449-56.

61. WHO: Hypertension <https://www.who.int/news/item/25-08-2021-more-than-700-million-people-with-untreated-hypertension>
62. WHO: More than 700 million people with untreated hypertension https://www.who.int/health-topics/hypertension#tab=tab_1
63. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *J Hypertens.* 2018;36(10):1953-2041.
64. Wilson PW, Cupples CF, Kannel WB. Is hyperglycemia associated with cardiovascular disease? The Framingham Study. *Amer. Heart J.* 1991;121:586-90.
65. Zachrisson K, Herlitz H, Lönn L, et al. Duplex ultrasound for identifying renal artery stenosis: direct criteria re-evaluated. *Acta Radiol.* 2017 Feb;58(2):176-82. doi:10.1177/0284185116641345.