UZBEKISTAN REPUBLIC HEALTHCARE MINISTRY

SAMARKAND STATE MEDICAL UNIVERSITY

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CLINICAL-IMMUNOLOGICAL STATUS IN THE DESTABILIZATION OF ISCHEMIC HEART DISEASE IN YOUNG PATIENTS AND WAYS OF ITS CORRECTION

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(monograph)

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In this monograph, the authors present contemporary findings on the clinical and immunological aspects of coronary heart disease in young patients. They explore the etiopathogenetic risk factors underlying the disease's development, with a particular focus on dyslipidemia and cytokine imbalance. The monograph incorporates recent scholarly works from CIS countries and abroad. Through their review of existing literature, the authors have identified several factors that predispose individuals, especially at a young age, to coronary heart disease. Dyslipidemia and cytokine imbalance are highlighted as the key etiopathogenetic drivers. Building upon their own clinical and laboratory research, the authors have further described the specific patterns of coronary heart disease in young patients, correlating them with these etiopathogenetic risk factors.

ACCEPTED ABBREVIATIONS

IL-	Interleukin
NO -	nitrogen oxide
TNF-α -	Tumor necrosis factor-α
ASB-	atherosclerotic plaque
AH -	arterial hypertension
AD -	blood pressure
AO -	aorta
ATP -	adenosine triphosphate
ARA II	angiotensin receptor antagonists **II**
WHO -	World Health Organization
Air Force -	first-time angina
GB -	hypertensive disease
DAD -	diastolic blood pressure
DLP	dyslipidemia
DNA -	deoxyribonucleic acid
IBS -	ischemic heart disease
BMI -	index mass body
IMMLJ	left ventricular myocardial mass index
CA -	coronary artery
CAG -	coronary angiography
CoefA-	atherogenicity coefficient
KBZ-	coronary heart disease
KVZ -	cardiovascular diseases
KVO -	cardovascular complications
KDO -	final diastolic volume
CDR -	final diastolic size
CSR -	final systolic size
KSO -	final systolic volume
CFC -	creatine phosphokinase
KFC-MV -	creatine phosphokinase metabolic protein
LJ -	left ventricle
HDL-	high-density lipoprotein
LPNP -	low-density lipoprotein
LDL-C -	very low-density lipoprotein
mRNA	matrix ribonucleic acid
MMP -	interventricular septum
MS -	metabolic syndrome
HBC-	unstable variants of angina
NFA -	low physical activity
OIM -	acute myocardial infarction
OKS-	acute coronary syndrome
OKSPST-	acute coronary syndrome with ST elevation
OKSdST-	acute coronary syndrome with ST segment depression

OSN -	acute heart failure
OXS -	total cholesterol
PIX-	post-infarction cardiosclerosis
PSN -	progressive angina pectoris
PDRF -	polymorphism of long restrictive fragments
PCR -	polymerase chain reaction
RF -	Russian Federation
САД -	systolic blood pressure
SD -	diabetes mellitus
CFT -	glomerular filtration rate
RSCEMC CRF	Samarkand Regional Branch of the Republican Scientific Center for Emergency Medical Care
TG-	triglycerides
TZSLV -	Left ventricle posterior wall thickness
TMP -	interventricular septum thickness
LVEF-	left ventricular ejection fraction
FR -	risk factors
CIN -	chronic heart failure
HR -	heart rate
ET-1 -	endothelin - 1
ED -	endothelial dysfunction

PREFACE

While developed economies are experiencing a general decline in mortality, coronary heart disease (CHD) stubbornly persists as a dominant force in morbidity, disability, and death. Acute myocardial infarction (AMI) alone contributes approximately 13% to the mortality toll from CHD. This grim reality is replicated in Uzbekistan, where cardiovascular diseases (CVD) are the primary cause of death, responsible for up to 60% of all fatalities. The impact of circulatory system diseases extends beyond healthcare, creating a profound socioeconomic problem by causing premature deaths among the young and productive. Myocardial infarction (MI) holds a central position in the statistics for initial disability and mortality, with a concerning trend of earlier disease onset. These combined factors have elevated the issues of coronary heart disease and acute intestinal infections beyond the realm of clinical medicine, framing them as matters of national security. Disturbingly, the mortality rate among young individuals diagnosed with coronary heart disease has reached an alarming 30% in the last 15 years, even when utilizing modern treatment approaches.

Acute myocardial infarction is the most severe and life-threatening acute manifestation of coronary artery disease, the pathogenetic basis of which in the vast majority of cases is the destabilization of the atherosclerotic plaque in the coronary artery system [40, 121, 231, 297]. In connection with the above, a comprehensive study of modern risk factors, as well as their combinations in young and middle-aged patients with coronary artery disease complicated by MI, is of particular scientific and practical importance. The data obtained during such studies can serve as a basis for optimizing approaches to primary and secondary prevention of myocardial infarction in this age group.

Over the past several decades, there's been a noticeable rise in the occurrence of risk elements linked to the onset of cardiovascular ailments. Considering the observed trend of coronary heart disease appearing at younger ages, adaptable lifestyle choices play a crucial role in how the illness develops. These include

smoking, poor dietary habits, insufficient physical activity, challenging work environments, and ongoing psychological stress. The cumulative impact of these elements fosters the development of obesity, abnormal lipid levels, diabetes, and the premature emergence of high blood pressure.

One of the leading pathogenetic mechanisms for the development of coronary heart disease is lipid metabolism disorders, characterized by an increase in the content of atherogenic lipoprotein fractions in blood plasma.

Current scientific data indicate the key role of inflammatory processes in the vessel wall in the initiation, progression, and destabilization of atherosclerotic lesions. Cytokines play a central role in regulating the inflammatory response in atherosclerosis, and their imbalance is accompanied by an increase in the levels of pro-inflammatory mediators - tumor necrosis factor α (TNF-α), interleukins IL-1β and IL-6 - while simultaneously reducing the production of anti-inflammatory interleukins (IL-4, IL-8, IL-10). Hyperexpression of pro-inflammatory cytokines is associated with accelerated progression of coronary heart disease and increased risk of developing acute cardiovascular complications.

Currently, the development of domestic healthcare is aimed at implementing comprehensive measures aimed at improving the early diagnosis of cardiovascular diseases, introducing modern preventive and treatment technologies, and adapting the healthcare system to international standards. Significant importance is attached to conducting regular medical examinations of the population to identify risk factors for the development of cardiovascular diseases. In this context, the timely identification of risk factors contributing to the early development of cardiovascular diseases in young people is one of the priority tasks of modern cardiology and is the basis for developing and implementing personalized preventive strategies.

CHAPTER 1.
Literature review

Contemporary epidemiological perspectives concerning ischemic heart disease in younger individuals.

The combination of modern clinical and population studies allows us to note the unfavorable dynamics of indicators characterizing the prevalence, loss of work capacity, and mortality due to coronary heart disease (CHD) in the populations of the CIS countries. A particular concern is the shift in the onset of the disease to earlier age groups, which indicates changes in the natural course of the pathology. Cardiovascular disease occupies a consistently high position among the nosological forms of cardiovascular pathology and is widely represented both in countries with a high level of economic development and in developing economies.

Results of long-term observations indicate the presence of clinical manifestations of coronary heart disease in a significant portion of the young male population, and the frequency of the disease in the age range of 20-44 years varies within 5-8%. The mortality rate from coronary heart disease in the 25-34 age group reaches two-digit values per 100,000 population and demonstrates a gradual increase. In the structure of overall mortality, a significant share is made up of people of working age, and male mortality in this cohort is many times higher than similar indicators in women [2]. The growing incidence of coronary heart disease in those under 45 significantly undermines both public health infrastructure and broader societal progress.

Gender differences in the frequency and timing of manifestations of coronary artery disease are pronounced. Women tend to develop this illness with a delay compared to men. Nevertheless, it remains a primary cause of death in older age brackets. RHD is diagnosed more often in men prior to old age, but its occurrence in women escalates in later life. Atherosclerotic changes in the arterial walls, the basis of

coronary artery disease, are primarily identified in younger and middle-aged people. The chronic manifestation of coronary heart disease is most characteristically associated with stable angina pectoris, a condition whose diagnosis is significantly informed by clinical examination findings. Analysis of the patient's subjective sensations, including the provoking factors, duration, and intensity of the pain syndrome, allows for the differentiation of ischemic pain from other forms of torakalgia. The physiopathological substrate of angina is a transient decrease in coronary blood flow, leading to a discrepancy between the metabolic needs of the myocardium and the level of its oxygen supply against the background of atherosclerotic or functional damage to the coronary arteries. The presence of angina is considered a marker of increased cardiovascular risk, and the unfavorable prognostic value of this syndrome is more pronounced in men [35].

The course of coronary heart disease in young age is characterized by clinical atypia and limited severity of prodromal symptoms. For a substantial number of patients, the disease's debut is not characterized by typical angina. Rather, it often begins with an acute coronary syndrome, most frequently manifesting as an acute myocardial infarction [75-78].According to coronary angiographic studies, in patients younger than 45 years old, stable angina is detected significantly less frequently compared to older age categories, while the frequency of primary detection of coronary artery disease at the stage of coronary artery disease is significantly higher [80].

"Additional analyses substantiate that younger individuals (under 40) often experience myocardial infarctions without any prior symptomatic ischemia. Should a pain syndrome present, its occurrences are generally fleeting and precede the acute episode by a short duration [77, 78]."The results of multicenter observations indicate a higher prevalence of painless forms of MI among young women compared to men, with no significant differences in the degree of coronary artery damage and biochemical markers of myocardial necrosis [80].

A significant problem of clinical practice in young patients remains the differential diagnosis of acute myocardial infarction and inflammatory myocardial lesions. The clinical presentation of myocarditis often mimics that of coronary artery stenosis, occurring when there is no hemodynamically significant narrowing of the coronary arteries. Specialized investigations have revealed that among younger patients who exhibit symptoms suggestive of coronary artery disease but have unobstructed coronary arteries, myocarditis can be identified in as many as 70% of instances [80, 81].

 Traditionally, ischemic heart disease (IHD) was considered a pathology of later life; however, its presence in younger patients has been on the rise in recent decades.

 IHD has typically been linked to older age, but its occurrence among younger patients has shown an increasing trend over the past few decades.

 The demographic profile of ischemic heart disease (IHD) is shifting; while once primarily seen in the elderly, its prevalence among younger patients has been expanding in recent decades.

By "young" in most epidemiological studies, people under 45, and sometimes up to 40 or even 35 years old, are understood. Early development of coronary artery disease has significant medical and socio-economic consequences, as it leads to loss of working capacity, decreased quality of life, and increased risk of premature death.

Modern epidemiological data indicate that the proportion of young patients among all cases of acute coronary syndrome is approximately 5-10%, with an increasing trend. Men get sick significantly more often than women, however, young women are often diagnosed with coronary artery disease later and have an atypical course, which worsens the prognosis.

Geographic differences in the prevalence of coronary heart disease among young people are observed in various regions of the world, reflecting the influence of socio-economic factors, lifestyle, and accessibility of medical care. In countries with a high level of urbanization, early onset of the atherosclerotic process is observed.

In young patients, coronary artery disease is often characterized by less pronounced, but more "unstable" atherosclerosis. Often, damage to one coronary artery is detected, however, the risk of thrombosis can be high. In a number of cases, coronary artery disease develops against the background of coronary spasm, coronary artery dissection, or thrombophilic conditions, rather than classical atherosclerosis. The clinical picture in young people can be atypical, which makes timely diagnosis difficult and leads to delayed treatment.

Cardiovascular disease in young patients is a pressing and growing problem in modern cardiology. Epidemiological data indicate changes in the structure of risk factors and the need to revise early diagnosis and prevention strategies. A comprehensive approach, including medical, behavioral, and social measures, is key to reducing morbidity and improving the prognosis in this population.

The significant burden of coronary heart disease, evidenced by its high prevalence, its contribution to premature mortality, and its lasting impact on individuals' ability to work, positions it as a critical medical and social concern today [10,12,54,105].The vast majority of deaths from cardiovascular diseases are recorded in low- and middle-income countries [87]. Despite significant progress in the field of preventive and therapeutic technologies, the disease continues to occupy a leading position in the structure of cardiovascular pathology. The identified features of the course of YUIK in young patients necessitate the development of differentiated and methodologically justified approaches to the organization of medical care for this category of patients.

Modern views on the etiological causes of coronary artery disease in young people

The increase in the prevalence of coronary heart disease (CHD) is due to both age-related changes affecting the cardiovascular system and the high frequency of risk factors (RF) that form an unfavorable cardiometabolic profile. It has been established that in younger men, arterial hypertension and diabetes

mellitus are detected less frequently compared to representatives of the middle age group, while obesity, smoking, and lipid metabolism disorders are recorded significantly more frequently. These circumstances determine the need to shift the emphasis of modern cardiology from isolated search for etiological factors to a comprehensive assessment of the combined impact of RF on morbidity and mortality from coronary heart disease in various age groups, with particular attention to the younger contingent of patients. Coronary artery disease (CAD) has traditionally been viewed as a disorder primarily affecting older adults. Nevertheless, over the past few years, there's been a heightened understanding of its presence in younger individuals. A significant number of studies label patients under 45 as "young," and some research employs even more restrictive age boundaries, such as 40 or 35.Early development of CAD is linked to notable health complications, prolonged disability, and significant economic impacts. Contemporary investigations now focus more intensively on identifying the distinct causative factors underlying CAD in younger groups.

Classic cardiovascular risk factors continue to play a major role in the onset of CAD among younger people, though their effects may vary somewhat from those observed in older patients.

Tobacco use stands out as the most dominant and consistently reported cause in young CAD sufferers, owing to its roles in promoting clot formation, damaging the vascular endothelium, and triggering inflammation, all of which hasten atherosclerosis.

Abnormal lipid profiles, especially elevated levels of low-density lipoprotein (LDL) cholesterol, are crucial contributors. Genetic conditions like familial hypercholesterolemia hold particular significance in premature CAD cases.

High blood pressure, which frequently goes undetected in younger adults, contributes to vascular injury and endothelial dysfunction early on.

Diabetes mellitus—especially type 2—is increasingly common in younger demographics and significantly elevates cardiovascular risk.

Excess body weight and physical inactivity foster metabolic imbalances that accelerate atherogenic processes from an early age.

A genetic predisposition constitutes a fundamental factor in CAD among young individuals. Having a family history of early cardiovascular disease dramatically increases vulnerability. Both monogenic disorders such as familial hypercholesterolemia and complex polygenic risk patterns have become more appreciated due to advancements in genetic diagnostics. These inherited factors often interact with external environmental triggers, precipitating early onset of the disease.

In contrast to older patients, young people may develop CAD through mechanisms other than atherosclerosis, which have gained wider recognition in contemporary cardiology. Examples include:

- Spontaneous coronary artery dissection, especially prevalent among young women;
- Coronary artery spasms, frequently linked to smoking or substance abuse;
- Congenital abnormalities of coronary anatomy;
- Hypercoagulable conditions and inherited or acquired thrombophilias;
- Inflammatory and autoimmune disorders, such as systemic lupus erythematosus or vasculitis.

These causes can provoke acute coronary syndromes even when significant atherosclerotic plaques are absent.

Current perspectives highlight the critical role played by psychosocial and lifestyle factors in the emergence of CAD within younger populations. Persistent stress, mood disorders like depression and anxiety, sleep disturbances, and unfavorable socioeconomic conditions are recognized as important elements influencing cardiovascular health early in life.

Modern studies show that the increase in the burden of coronary artery disease is closely related to the phenomenon of FR accumulation in one individual. It has been shown that among hospitalized patients with coronary artery disease, the presence of at least one RF is detected in more than 90% of patients, a combination

of two RFs - in approximately 70% of patients, and three or more - in more than one-third of patients, regardless of gender. At the same time, the simultaneous presence of several RFs has a cumulative effect, significantly increasing the likelihood of disease development and death. Previously, it was demonstrated that the combination of two or three RFs significantly increases the risk of death from coronary heart disease, which formed the basis for the concept of the total cardiovascular risk.

RMS is traditionally divided into modifiable and non-modifiable. The latter include age, male sex, and a complicated family history of cardiovascular diseases. Modified RFs include arterial hypertension, lipid metabolism disorders, diabetes mellitus, abdominal obesity, smoking, alcohol consumption, and low physical activity. Epidemiological data indicate a high prevalence of these RFs already at a young age, while their combination forms an unfavorable prognostic background.

The influence of multiple RFs on the severity of atherosclerotic lesions of coronary arteries deserves special attention. It has been shown that in young individuals with diabetes mellitus and a combination of several RFs, multiple vascular lesions of the coronary artery are more common. Morphological studies conducted in young individuals demonstrated a direct correlation between the frequency of RF and the area of atherosclerotic lesions of the aorta and coronary arteries. With an increase in the frequency of fractures, a progressive increase in both fat strips and formed atherosclerotic plaques was observed, indicating the early onset and accelerated course of atherogenesis.

The age factor can enhance the negative impact of modified RFs. Elevated blood pressure and cholesterol levels in young and middle-aged individuals are associated with an increased risk of coronary events with age. At the same time, atherosclerotic lesions of the coronary arteries are more frequently detected in men and are characterized by greater severity in all age groups. With age, the absolute frequency of atherosclerosis increases, while the relative contribution of individual RFs may decrease, which is explained by the effect of selective survival.

Arterial hypertension remains one of the main determinants of the development of cardiovascular diseases, including coronary heart disease. The prevalence of elevated blood pressure increases with age and reaches maximum values in older age groups. Despite the successes achieved in blood pressure monitoring, exceeding the threshold values of systolic and diastolic blood pressure is associated with a twofold increase in the risk of developing acute myocardial infarction. Currently, arterial hypertension is considered not as an isolated RF, but as a component of an integral cardiovascular risk, especially in combination with other adverse factors.

Tobacco smoking, along with arterial hypertension, occupies one of the leading positions among behavioral RFs. The highest prevalence of smoking is recorded in young and middle age, with subsequent decrease in older groups. Despite the overall decrease in the number of smokers as a result of preventive programs, the influx of new tobacco consumers, including among young people, persists. It has been established that smoking significantly increases the risk of coronary events and cardiovascular mortality, and the severity of the risk increases proportionally to the intensity of smoking. Quitting smoking is associated with a significant decrease in mortality, including patients already diagnosed with coronary artery disease, regardless of gender and age.

Problems with lipid metabolism are a powerful driver in the development of coronary heart disease. With advancing age, the typical pattern for blood lipids involves an increase in total cholesterol, low-density lipoproteins, and triglycerides, alongside a decrease in high-density lipoproteins. These unfavorable shifts in the lipid profile manifest earlier in males, while in females, their severity escalates notably after menopause. The correlation between high cholesterol and the onset of coronary heart disease is most apparent in younger age groups, whereas in older individuals, its influence is partially offset by the survival effect. The combination of dyslipidemia with other RFs, especially arterial hypertension and smoking, increases the risk of a fatal outcome many times over.

Obesity is an independent and mediated RF of coronary artery disease, contributing to the formation of arterial hypertension, diabetes mellitus, and

atherogenic dyslipidemia. The prevalence of obesity has a pronounced age dependence, peaking in middle and old age. The continued escalation of obesity, notwithstanding existing preventative strategies, enables us to forecast a greater incidence of coronary heart disease. Abdominal obesity holds special significance, as its increasing frequency with age correlates with a heightened cardiovascular risk.

The role of moderate alcohol consumption in the development of coronary heart disease remains debatable. A number of studies indicate the possible protective effect of small doses of alcohol, implemented through anti-inflammatory, vasodilating, and anti-atherogenic mechanisms. At the same time, alcohol abuse is associated with an increase in cardiovascular morbidity and mortality, and the prevalence of its consumption varies significantly depending on gender, age, and socio-cultural factors.

Diabetes mellitus is less common in young patients with coronary artery disease, however, its presence significantly accelerates the progression of atherosclerosis and increases the risk of premature death. Metabolic disorders accompanying insulin resistance and hyperinsulinemia contribute to an increase in thrombogenic potential, endothelial dysfunction, and atherosclerotic plaque instability.

Psycho-emotional stress and chronic nervous exhaustion are considered significant non-modifiable risk components. The high prevalence of occupational and social stress is associated with the formation of anxiety-depressive disorders, which increase the likelihood of developing acute cardiovascular complications. An additional negative aspect of stress is its connection with the formation of unfavorable behavioral habits, including smoking, alcohol abuse, hypodynamia, and irrational nutrition.

Imbalanced nutrition, characterized by high intake of saturated fats, refined carbohydrates, and insufficient intake of vegetables and fruits, is an important determinant of metabolic disorders. Correcting the diet with increased consumption of foods rich in dietary fiber is associated with improved carbohydrate and lipid metabolism and reduced cardiovascular risk.

Thus, analyzing the living conditions, work activities, and health status of young people, as well as identifying the combined effects of modifiable and non-modifiable risk factors, is one of the key tasks of modern cardiology. Comprehensive study of risk factors for cardiovascular diseases in young people is of fundamental importance for preserving the labor and intellectual potential of society and justifying effective preventive strategies.

Modern views on the pathogenesis of heart disease in young people

Ischemic heart disease (IHD) is one of the leading causes of morbidity and mortality worldwide, including among young patients (Chen et al., 2022). While traditionally, coronary heart disease, traditionally viewed as a condition primarily affecting those in their middle and later years, has shown a recent shift in its demographic presentation. Over the past few decades, there's been an observable trend of the disease manifesting at younger ages, with initial clinical indicators of coronary heart disease now being observed in individuals under 45 years old (Roth et al., 2020). In young patients, coronary artery disease often has a more aggressive course, characterized by rapid progression of the atherosclerotic process, a high frequency of unstable angina, and an increased risk of early myocardial infarction (EMI) (Khera et al., 2019). Studying the characteristics of coronary heart disease in this age group is important for developing preventive and therapeutic strategies, as well as for reducing social and economic losses associated with premature disability.

According to the World Health Organization, coronary heart disease is the leading cause of death among people of working age. Among patients under 45, approximately 10-15% of all myocardial infarction cases are attributed to this age group (Yusuf et al., 2021).

The main risk factors for developing coronary heart disease in young patients are:

- Genetic predisposition (family history of early infarction),
- Dyslipidemia,
- Arterial hypertension

- Diabetes mellitus
- Obesity and metabolic syndrome,

Despite a relatively low prevalence among young people, the course of the disease in this group is characterized by a high frequency of complications and an unfavorable prognosis with untimely diagnosis.

At the heart of coronary artery disease lies coronary artery atherosclerosis, which develops due to chronic inflammation of the vascular endothelium, lipid metabolism disorders, and cytokine imbalance (Libby et al., 2019). In young patients, atherosclerotic changes are often combined with:

1. Cytokine imbalance, including elevated levels of pro-inflammatory cytokines (IL-1β, TNF-α, IL-6) and decreased levels of anti-inflammatory mediators (IL-10, IL-4), contributes to the formation of unstable plaques.
2. Genetic and metabolic factors, including the polymorphism of genes regulating lipid and carbohydrate metabolism.
3. Dyslipidemia, which manifests as an increase in LDL and triglyceride levels and a decrease in HDL.

A characteristic of young patients with coronary artery disease is the presence of a combination of risk factors that enhance atherogenesis, such as obesity against the background of smoking or hypertension (Khera et al., 2019).

In young patients with coronary artery disease, the following manifests:

- Angina - more often unstable or progressive,
- Myocardial infarction, including with minimal precursors,
- Episodes of sudden cardiac death, especially in combination with genetic predisposition and severe dyslipidemia.

The clinical picture can be atypical, with moderate pain or rapid fatigue during physical activity, which often leads to late diagnosis and worsening of the prognosis (Sharma et al., 2020).

Diagnostic approaches include:

- Laboratory studies, including lipid profile, inflammation markers, and cytokine status,

- ECG and stress tests,
- Echocardiography, which allows for the assessment of left ventricular function and the identification of hypokinesis zones,

Young patients often show unilateral lesions or unstable plaques, making early diagnosis particularly important.

Treatment of coronary artery disease in young patients should be comprehensive:

1. Correction of risk factors: weight control, smoking cessation, normalization of blood pressure and lipid metabolism.
2. Drug therapy, including:
   - Statin and other hypolipidemic drugs,
   - Antiplatelet agents (aspirin),
   - β-blockers and ACE inhibitors.
3. Use of anti-inflammatory strategies aimed at normalizing cytokine balance, which reduces the progression of atherosclerosis (Ridker et al., 2017).

Comprehensive therapy contributes not only to the reduction of clinical manifestations but also to improving the prognosis and quality of life of patients.

YUIK in young patients is of particular importance in terms of public health. Early manifestation of the disease leads to:

- Loss of working capacity,
- Increasing economic costs for medical services,
- Increased risk of early disability.

Timely identification of risk factors, lifestyle modification, and complex therapy significantly reduce the risk of adverse outcomes and improve the long-term prognosis (Roth et al., 2020).

In young patients, coronary heart disease is characterized by a high rate of progression and a complex clinical picture. The main mechanisms of pathogenesis are dyslipidemia, chronic inflammation, cytokine imbalance, and genetic predisposition. Early diagnosis, prevention of risk factors, and comprehensive

treatment significantly improve the prognosis and reduce the socio-economic burden of the disease.

In the system of pathogenetic mechanisms of coronary heart disease (CHD), lipid metabolism disorders, primarily dyslipidemia (DLP), play a leading prognostic role. DLP is understood as a condition characterized by a shift in the balance between atherogenic and anti-atherogenic lipoprotein fractions, in which the concentrations of blood plasma lipids and lipoproteins exceed physiological values [39, 136]. It has been established that DLP-associated subclinical atherosclerotic changes in coronary arteries form at a young age and progress asymptomatically for a long time, reaching practically ubiquitous prevalence by middle age, preceding the clinical manifestation of coronary artery disease [75, 141].

The presence of DLP in combination with other modifiable risk factors contributes to the accelerated formation of atherosclerotic plaques in the coronary artery and the earlier onset of the disease. In recent decades, priority attention has been given to the early detection and correction of hypercholesterolemia and elevated levels of low-density lipoproteins (LDL), which have pronounced atherogenic potential [4, 113, 133]. Modern data indicate that the combination of increased LDL concentration, an increase in the proportion of their small, dense particles, the growth of very low-density lipoproteins (LDL), and a decrease in the level of high-density lipoproteins (HDL) forms a lipid profile associated with a maximum risk of coronary atherosclerosis and its complications [70, 75, 113].

The results of epidemiological and clinical studies demonstrate a pronounced prophylactic effect in the correction of lipid disorders. Thus, a 10% decrease in the concentration of total plasma cholesterol is accompanied by a decrease in the frequency of coronary heart disease by approximately a quarter over the next five years, while a decrease in the level of LDL by 1 mmol/l is associated with a 20% reduction in the frequency of cardiovascular events [40, 136]. At the same time, lipid disorders are more frequently detected in young patients with coronary artery disease compared to older age groups, which emphasizes their special role in the formation of premature coronary pathology [147, 199]. The increase in total cholesterol is

among the leading contributing factors to the structure of premature mortality, reaching about 23%. A decrease in HDL levels is registered in approximately every fifth male, and hypertriglyceridemia in every third [70].

A characteristic feature of the lipid profile in young patients with coronary artery disease is the relatively low levels of HDL in combination with elevated triglyceride concentrations, which confirms the key role of LDL in the early development of the disease [79]. At the cellular level, in cases of lipid metabolism disorders, the smooth muscle cells of the vascular wall acquire the ability to capture modified LDL with subsequent transformation into foamy cells, which accelerates the progression of the atherosclerotic process [133].

Obesity is of particular importance in the formation of atherogenic DLP. Individuals with a body mass index of ≥30 kg/m2 often exhibit a characteristic lipid phenotype, including hypertriglyceridemia and a decrease in HDL levels [159]. Simultaneously, the increased release of free fatty acids from adipocytes leads to the activation of LDL synthesis in the liver, which exacerbates the imbalance of the blood lipid spectrum [24]. An additional pathogenetic mechanism is the decrease in the activity of peripheral lipoprotein lipase, which limits the catabolism of triglyceride-containing lipoproteins [147, 199].

Features of nutrition are a significant determinant of the level of blood lipids in young people. Including polyunsaturated fatty acids in the diet helps lower atherogenic fractions and raise HDL levels [22, 39, 107], while overindulging in trans fats is linked to higher LDL concentrations. Randomized clinical studies have shown that following a Mediterranean-based diet and a low-fat diet allows for a decrease in LDL levels by an average of 11% [22, 70, 161].

Clinical manifestations of dyslipidemia are distinguished by significant polymorphism - from complete absence of symptoms to classic external signs of lipid imbalance and hemodynamic manifestations of atherosclerosis. During physical examination of the patient, special attention should be paid to the detection of eye xanthelasms, which are flat or slightly raised yellowish-orange lesions, as well as to the examination of the extensor surfaces of the extremities and Achilles

tendons, where various types of xanthem can be localized. Tendon xanthomas, especially in the Achilles tendon region, are considered a highly specific sign of pronounced dyslipidemia, while eruptive xanthomas indicate severe hypertriglyceridemia [147, 199].

Additional indirect signs of lipid metabolism disorders can be the lipid arc of the cornea, as well as vascular murmurs detected during auscultation of the aorta and large arteries, due to atherosclerotic thickening of the vessel wall and the formation of stenosis. In patients with similar clinical findings, coronary heart disease often manifests at 30-40 years of age or even earlier [10, 40, 111].

Cardiovascular disease among younger populations has gained recognition as a significant clinical and public health concern, overturning the conventional belief that heart conditions predominantly affect older adults. In relevant studies, people under the age of 45 are often classified as young. Recent advancements in cardiovascular science have significantly increased our understanding of the development of heart disease in this population by revealing complex links between genetic predispositions, metabolic alterations, inflammatory events, and environmental factors.

Early Atherosclerosis and Endothelial Dysfunction

A key pathological factor in young patients is the premature appearance of endothelial dysfunction, marking the initial phase in the onset of many cardiovascular disorders. Risk exposures such as tobacco use, abnormal lipid levels, obesity, and high blood pressure reduce nitric oxide availability, increase oxidative damage, and provoke vascular inflammation. These events facilitate lipid deposition in arterial walls and speed up the early formation of atherosclerotic lesions.

Genetic and Molecular Mechanisms

Hereditary factors significantly contribute to heart disease etiology in young individuals. Single-gene conditions—like familial hypercholesterolemia and hereditary cardiomyopathies—directly trigger early manifestations of the disease. Moreover, multiple polygenic risk components affect lipid processing, vascular function, and inflammatory pathways.

Inflammation and Immune Dysregulation

Sustained low-level inflammation is increasingly acknowledged as a central contributor to heart disease among younger patients. Raised inflammatory biomarkers, activation of endothelial cells, and infiltration of immune cells contribute to the destabilization of atherosclerotic plaques and heart muscle damage. Autoimmune and systemic inflammatory disorders, such as systemic lupus erythematosus and rheumatoid arthritis, intensify cardiovascular risk by causing immune-driven vascular injury.

Metabolic and Hormonal Influences

Metabolic imbalances—including insulin resistance, excess body weight, and metabolic syndrome—play a major role in the development of cardiovascular disease in the young population. These states foster abnormal lipid profiles, oxidative stress, and widespread inflammation. Hormonal variations, particularly changes in cortisol and sex hormone levels, can also modify cardiovascular risk.

Non-Atherosclerotic Pathogenetic Mechanisms

In younger individuals, heart disease can also arise through non-atherosclerotic routes. Conditions such as coronary artery spasms, spontaneous coronary artery dissections, congenital abnormalities of coronary vessels, myocarditis, and inherited rhythm disorders represent important underlying mechanisms. Additionally, states of increased blood clotting and endothelial injury may precipitate cardiovascular events independent of atherosclerosis.

Lifestyle and Environmental Factors

Lifestyle choices and environmental exposures play a pivotal role in the development of heart disease in young individuals. Air pollution, exposure to fine particulate matter (PM2.5), and occupational hazards (e.g., shift work, prolonged stress) further exacerbate cardiovascular risk by promoting oxidative stress, endothelial dysfunction, and systemic inflammation. Additionally, psychosocial factors such as chronic stress, depression, and socioeconomic disparities influence cardiovascular health through neurohormonal dysregulation and unhealthy coping mechanisms (e.g., smoking, overeating).

Emerging Risk Factors and Novel Biomarkers

Recent research has identified novel risk factors and biomarkers that may predict early cardiovascular disease in young adults. Elevated levels of lipoprotein(a) [Lp(a)], a genetically determined lipoprotein, are strongly associated with premature atherosclerosis. Advanced glycation end-products (AGEs), markers of oxidative stress, and circulating microRNAs (e.g., miR-126, miR-21) have emerged as potential indicators of endothelial dysfunction and plaque instability. Furthermore, gut microbiota dysbiosis has been linked to metabolic syndrome, inflammation, and atherosclerosis, suggesting a role for the microbiome in cardiovascular health.

Diagnostic and Therapeutic Challenges

Diagnosing heart disease in young individuals presents unique challenges due to atypical symptom presentation, underrecognition of risk factors, and limited awareness among healthcare providers. Many young patients with acute coronary syndromes (e.g., myocardial infarction) may not exhibit classic symptoms such as chest pain, leading to delayed diagnosis. Early intervention with statins, anti-inflammatory therapies (e.g., colchicine, canakinumab), and lifestyle modifications can mitigate disease progression, but adherence remains a significant barrier.

Prevention and Public Health Strategies

Preventive strategies targeting young populations are critical to reducing the burden of cardiovascular disease. Public health initiatives should focus on:

- Education and Awareness: Promoting cardiovascular health literacy, particularly regarding modifiable risk factors (smoking, diet, physical inactivity).
- Early Screening: Implementing risk stratification tools (e.g., Framingham Risk Score, polygenic risk scores) to identify high-risk individuals.
- Policy Interventions: Regulating tobacco and alcohol use, improving air quality, and promoting workplace wellness programs.
- Personalized Medicine: Leveraging genetic and molecular data to tailor prevention and treatment strategies.

Future Directions and Research Priorities

Future research should focus on:

- Precision Medicine: Identifying genetic and epigenetic biomarkers to predict and prevent early-onset heart disease.
- Immune Modulation: Exploring targeted therapies for inflammatory and autoimmune-mediated cardiovascular damage.
- Digital Health: Utilizing wearable devices and AI-driven analytics for early detection and monitoring.
- Global Disparities: Addressing socioeconomic and geographic variations in cardiovascular risk and access to care.

Heart disease in young people is a complex, multifactorial condition driven by genetic, metabolic, inflammatory, and environmental factors. Early detection, personalized prevention, and innovative therapies are essential to mitigating this growing public health challenge. A multidisciplinary approach—integrating clinical, molecular, and public health strategies—will be key to improving outcomes in this vulnerable population.

Currently, one of the priority tasks of cardiology is the development and implementation of effective strategies for early diagnosis, prevention, and pathogenetically justified correction of atherogenic forms of dyslipidemia. Studying subclinical atherosclerosis is of particular importance, as timely detection and treatment of lipid disorders in the early stages of the pathological process can either prevent its further development or significantly slow its progression. In this regard, the formation of optimal diagnostic and treatment algorithms is considered a key direction in reducing the burden of atherosclerotic cardiovascular diseases.

The role of immune imbalance in the pathogenesis of coronary artery disease in young patients

Cardiovascular disease is one of the most common cardiovascular pathologies and develops primarily as a result of atherosclerotic damage to the coronary artery. The disease is characterized by a chronic course with a periodic change in the phases of clinical stabilization and exacerbation, reflecting the dynamics of pathological processes in the vessel wall. Modern understanding of the pathogenesis of coronary

artery disease is increasingly based on the inflammatory concept, according to which local and systemic immune-inflammatory reactions play a key role in the initiation, progression, and complication of atherosclerosis.

Atherosclerotic lesions of the coronary arteries are a prolonged inflammatory process accompanied by an infiltration of the vascular wall by immune system cells, including T-lymphocytes and macrophages. These cells participate both in the accumulation of lipids in the extracellular and intracellular spaces and in the formation of early atherosclerotic changes. The combined effect of these mediators contributes to the growth and destabilization of the atherosclerotic plaque, which increases the likelihood of thrombotic coronary occlusion.

In recent years, special attention has been paid to the study of cytokines as molecular markers of inflammatory activity in atherosclerosis. Cytokines are low molecular weight regulatory proteins synthesized by a wide range of cells, including elements of the immune system, endothelium, connective tissue cells, and epithelium. They provide intercellular communication and coordinate inflammatory, immune, and reparative processes.

In the context of atherogenesis, cytokines are conventionally divided into pro- and anti-inflammatory. Tumor necrosis factor and interleukins, which aid in the maintenance of inflammatory activity and harm to the vascular wall, are included in the first group, whereas anti-inflammatory cytokines reduce the intensity of the immune response and help stabilize the atherosclerotic process. The clinical course and prognosis of coronary artery disease are largely determined by the balance between these functionally opposite groups of mediators.

Cytokines are characterized by high biological activity and act in minimal concentrations, exerting both enhancing and inhibiting effects on each other. Their synthesis is, as a rule, transient and is strictly regulated. Disruption of cytokine production regulation mechanisms plays a significant role in the formation of both physiological and pathological conditions.

The main source of pro-inflammatory cytokines in atherosclerosis is activated lymphocytes and macrophages. In the zone of atherosclerotic plaque formation, they

stimulate the adhesion of leukocytes to the endothelium, enhance the interaction of endothelial cells with atherogenic lipoproteins, and contribute to the transition of the endothelium to a prothrombotic state. As the disease progresses, pro-inflammatory mediators activate the cascade of coagulation, enhance the degradation of the intercellular matrix, and contribute to the formation of fibrous changes in the vascular wall.

Anti-inflammatory cytokines, on the contrary, perform a regulatory function, limiting the excessive inflammatory reaction and reducing the degree of tissue damage. Imbalance, characterized by the predominance of pro-inflammatory factors against a background of decreased anti-inflammatory activity, is associated with an unfavorable prognosis and a high risk of cardiovascular complications.

Interleukin-1β plays a central role in the inflammatory cascade, possessing pronounced pro-inflammatory and immunomodulatory activity. Disruption of its synthesis regulation is considered one of the triggers of pathological changes in coronary heart disease. The sources of IL-1β are monocytes, macrophages, neutrophils, endothelial and lymphoid cells. The interaction of this cytokine with receptor complexes on the cell surface initiates intracellular signaling pathways, leading to the activation of the inflammatory response.

Ischemic heart disease (IHD) in young patients is a significant problem in modern healthcare, given the increasing number of cases of early manifestation of the disease. According to the World Health Organization (WHO), approximately 10-15% of all myocardial infarctions occur in individuals under 45 years of age (Roth et al., 2020). Despite their relatively young age, the course of the disease in this group is characterized by a high rate of progression, as well as a predisposition to early coronary complications.

In recent years, researchers have focused on the role of immune mechanisms and inflammatory processes in the pathogenesis of coronary artery disease. Disruptions in the balance between the pro- and anti-inflammatory components of the immune system (immune imbalance) are considered a key factor contributing to

the formation of atherosclerotic plaques and their instability in young patients (Libby et al., 2019; Khera et al., 2019).

Younger people are experiencing an increasing number of instances of coron ary artery disease (CAD), which has different pathogenic characteristics than CAD in older people. Growing data indicate that disruptions in immune system balance are crucial contributors to the onset and advancement of CAD in this demographic. Recent studies emphasize the roles of persistent inflammation, disordered innate and adaptive immune responses, and the interactions between immune and metabolic systems as major factors driving early coronary artery disease.

Activation of Innate Immunity and Associated Inflammation

The innate immune response is a key initiator in the development of atherosclerosis. In young patients, damage to the endothelium from factors like smoking, abnormal lipid profiles, metabolic dysfunctions, or psychological stress leads to the stimulation of innate immune cells, including monocytes and macrophages. These immune cells invade the arterial walls and stimulate the secretion of inflammatory molecules such as tumor necrosis factor-alpha, interleukin-1 beta, and interleukin-6. Continuous activation of these pathways contributes to endothelial impairment, lipid buildup, and the early emergence of arterial plaques.

Dysfunction of Adaptive Immune Responses

The adaptive immune system also plays a vital role in young-onset CAD. Pro-inflammatory T cell subsets, especially T helper 1 (Th1) and Th17 cells, promote vascular inflammation and plaque vulnerability. On the other hand, regulatory T cells (Tregs), which normally provide anti-inflammatory protection, are often diminished in function or number. B cells further influence the disease process through antibody production and the release of cytokines, which shape inflammatory signaling within atherosclerotic sites.

Impact of Autoimmune and Chronic Inflammatory Disorders

Individuals with early CAD frequently have concurrent autoimmune or long-standing inflammatory diseases, such as systemic lupus erythematosus, rheumatoid

arthritis, or inflammatory bowel disease. In these cases, immune-mediated injury to blood vessels, deposition of immune complexes, and ongoing systemic inflammation accelerate atherosclerotic changes beyond what is explained by classic cardiovascular risk factors. This supports the idea that immune dysregulation alone can substantially drive CAD development.

Interplay Between Immune and Metabolic Systems

In young CAD patients, imbalances in immune responses are closely intertwined with metabolic problems. Conditions like obesity, insulin resistance, and metabolic syndrome foster a pro-inflammatory immune profile characterized by macrophages adopting a disease-promoting phenotype and heightened cytokine secretion. Fat tissue functions as an active immunological organ, producing adipokines that affect immune cell behavior and contribute to inflammation within vascular tissues.

Plaque Vulnerability and Thrombosis

Beyond promoting plaque build-up, immune system disturbances contribute to plaque destabilization and the risk of thrombosis. The fibrous cap that covers atherosclerotic plaques is broken down by enzymes released by immune cells, such as matrix metalloproteinases, making them more susceptible to rupture.

This rupture exposes thrombogenic material to the bloodstream, triggering platelet aggregation and thrombus formation, events that can precipitate acute coronary syndromes even in younger patients. Furthermore, pro-inflammatory cytokines enhance the expression of tissue factor and other coagulation molecules, promoting a hypercoagulable state that further elevates thrombotic risk.

Therapeutic Implications and Future Directions

Recognizing the critical role of immune imbalance in early-onset CAD provides novel opportunities for therapeutic intervention. Targeting inflammatory pathways through agents such as interleukin-1β inhibitors (e.g., canakinumab) or modulating immune cell function holds promise in altering disease progression. Additionally, lifestyle modifications and pharmacologic management aimed at correcting metabolic dysfunctions may beneficially affect immune profiles. Future

research focusing on identifying specific immune signatures and biomarkers in young CAD patients will enhance risk stratification and allow personalized immunomodulatory treatments.

Immune dysregulation, encompassing aberrant innate and adaptive responses, autoimmune influences, and immune–metabolic crosstalk, plays a central role in the pathogenesis of coronary artery disease in young individuals. These mechanisms not only drive early atherogenesis but also contribute to plaque instability and thrombotic complications. A comprehensive understanding of immune involvement offers the potential for more effective prevention and management strategies tailored to this distinct patient population.

In coronary artery disease, a disturbed immune equilibrium is primarily observed through:

1. Elevated pro-inflammatory signaling molecules:
   - Prominent players include IL-1β, IL-6, TNF-α, and IL-18.
   - These molecules trigger endothelial cells, boost the display of adhesion molecules, and encourage the movement of monocytes and macrophages into the artery walls. This process fuels the development of atherosclerotic lesions (Ridker et al., 2017).
2. Diminished anti-inflammatory signaling molecule activity:
   - IL-10, IL-4, and TGF-β are crucial for maintaining the stability of atherosclerotic plaques.
   - A reduction in these molecules exacerbates inflammatory processes, leads to the breakdown of structural components, and heightens the danger of plaque rupture (Libby et al., 2019).
3. Compromised immune cell function:
   - In younger individuals with coronary artery disease, T-lymphocytes and macrophages show heightened activity, releasing pro-inflammatory signals.
   - Concurrently, the effectiveness of regulatory T-cells (Treg) declines, impairing the body's ability to control inflammation and accelerating the progression of atherosclerosis (Khera et al., 2019).

Collectively, this immune dysregulation establishes a persistent inflammatory environment, contributing to the early onset of atherosclerotic changes, even in young patients presenting with relatively mild symptoms.

Research indicates a direct relationship between the levels of pro-inflammatory cytokines and the extent of atherosclerotic damage:

- **IL-1β:** Found in higher amounts in young patients experiencing unstable angina, particularly when LDL cholesterol levels are elevated (Yamagishi et al., 2021).
- **IL-6:** Contributes to the production of C-reactive protein and promotes platelet aggregation, thereby increasing the risk of acute coronary events.
- **TNF-α:** Induces programmed cell death in endothelial cells and compromises the integrity of the vascular wall, making thrombus formation more likely (Ridker et al., 2017).

Simultaneously, a decrease in IL-10 and TGF-β impairs the stabilization of atherosclerotic plaques and raises the likelihood of their rupture, a concern particularly for younger individuals with significant metabolic risk factors (Libby et al., 2019).

This immune dysregulation creates a "progressive inflammatory background," which contributes to the early development of atherosclerotic changes even with relatively mild clinical manifestations in young patients.

Studies show that the level of pro-inflammatory cytokines correlates with the severity of atherosclerotic changes:

- **IL-1β:** increased in young patients with unstable angina, especially with high levels of LDL (Yamagishi et al., 2021).
- **IL-6:** promotes C-reactive protein synthesis and stimulates platelet formation, increasing the risk of acute coronary syndromes.
- **TNF-α:** induces apoptosis of endothelial cells and disrupts the function of the vascular wall, which increases the likelihood of thrombus formation (Ridker et al., 2017).

At the same time, a decrease in IL-10 and TGF-β leads to a disruption in the stabilization of atherosclerotic plaques and an increased risk of their rupture, which is especially relevant for young patients with a high metabolic risk (Libby et al., 2019).

The interplay between these pro- and anti-inflammatory factors dictates the overall inflammatory tone within the arterial wall. When pro-inflammatory signals dominate, they initiate and perpetuate a cascade of events that promote plaque growth and instability. Conversely, a deficiency in anti-inflammatory cytokines leaves the system vulnerable to unchecked inflammation and plaque erosion. This delicate balance is crucial for maintaining vascular health, and its disruption is a hallmark of immune involvement in CAD. The heightened inflammatory state can also influence other cardiovascular risk factors, creating a vicious cycle that accelerates disease progression. For instance, chronic inflammation can contribute to insulin resistance and dyslipidemia, further exacerbating the atherosclerotic process.

The influence of immune system dysfunction on the emergence of coronary artery disease in individuals of younger age groups. Imbalances in the immune system lead to: Development of vulnerable atherosclerotic plaques prone to breakage and clot development. Rapid worsening of lipid abnormalities due to heightened macrophage activity and amplified endothelial cell damage. A heightened susceptibility to premature heart attacks and unstable angina has been observed clinically (Sharma et al., 2020). Younger individuals may exhibit a greater influence of immune responses in the development of atherosclerosis, which progresses more rapidly due to a combination of genetic predispositions and lipid abnormalities. Restoring immune system equilibrium holds significant potential for both preventing and managing coronary heart disease.

Therapeutic approaches aimed at reducing inflammation, such as employing interleukin-1β blockers like kanakinumab, have demonstrated a lower incidence of cardiovascular complications in individuals suffering from atherosclerosis (Ridker et al., 2017).

· Modulation of Treg cell activity and normalization of the Th1/Th2 ratio can slow the progression of atherosclerosis.

· Complex therapy with lipid metabolism correction further reduces the pro-inflammatory background and prevents acute coronary events.

These approaches are especially relevant for young patients, in whom early intervention can prevent long-term complications and disability.

Immune imbalance plays a key role in the pathogenesis of coronary artery disease in young patients, determining the rate of progression of atherosclerotic changes and the risk of early complications. Increased activity of pro-inflammatory cytokines, decreased activity of anti-inflammatory mediators, and dysfunction of immune cells create an inflammatory background that accelerates the formation of unstable atherosclerotic plaques. Early diagnosis of immune imbalance disorders and their correction in combination with lifestyle changes and lipid metabolism control is a promising strategy for reducing morbidity and improving prognosis in this group of patients.

IL-1β has a multifaceted effect on the vascular wall: it enhances the expression of adhesion molecules, stimulates leukocyte migration, increases the activity of metalloproteinases, and promotes the proliferation of smooth muscle cells. These effects lead to thinning of the fibrous covering of the atherosclerotic plaque and increase the likelihood of its rupture. In addition.

Elevated IL-1β concentrations are associated with impaired coronary blood flow and the development of myocardial ischemia. Conversely, the suppression of its production is accompanied by a decrease in inflammatory activity, a reduction in oxidative stress, and the restoration of the functional state of the endothelium. Clinical studies show a significant increase in the level of IL-1β in patients with acute forms of coronary artery disease compared to the stable course of the disease and healthy individuals, which confirms its prognostic significance.

Anti-inflammatory interleukin-10 plays a key role in limiting the inflammatory process and stabilizing the atherosclerotic plaque. It is synthesized by

activated immune cells and has the ability to suppress the expression of pro-inflammatory cytokines, reduce the activity of macrophages, and suppress thrombotic mechanisms. Due to these effects, IL-10 is considered one of the factors of cardioprotection.

IL-10 promotes the preservation of endothelial function, reduces the severity of oxidative stress, and supports nitrogen oxide synthesis. In addition, it participates in the regulation of blood fibrinolytic activity, providing an anticoagulant effect. Clinical observations indicate a decrease in IL-10 levels in unstable forms of coronary artery disease, with minimal values detected in patients with acute myocardial infarction.

Maintaining low IL-10 concentration against the background of ongoing therapy is considered a sign of ongoing inflammatory process in the atherosclerotic plaque and is associated with an increased risk of recurrence of acute coronary events. Conversely, effective treatment, including reperfusion methods, is accompanied by the restoration of cytokine balance and a decrease in systemic inflammation.

The activation of endothelial cells is also an important component of the destabilization of the atherosclerotic process. During inflammation, the endothelium starts to actively produce growth factors, chemokines, and cytokines, which helps to maintain immune inflammation and promote endothelial dysfunction.

The pathogenetic unity of these processes in coronary artery disease is highlighted by the intimate link between endothelial dysfunction and the activity of proinflammatory cytokines.

Thus, inflammation plays a central role in the pathogenesis of coronary artery atherosclerosis. The shift of cytokine balance towards pro-inflammatory activity, primarily due to the hyperproduction of IL-1β and a decrease in the level of IL-10, contributes to the progression of the disease, the aggravation of myocardial ischemia, and the development of adverse cardiovascular outcomes. In this regard, one of the top priorities of contemporary cardiology is thought to be the

creation of methods for the early diagnosis and pathogenetic management of cytokine status, particularly in young patients.

Proactive intervention methods are vital for younger patients facing cardiova scular issues, as prompt recognition and management of harmful mechanisms can dramatically influence the course of the disease. In contrast to older age groups, yo uthful individuals possess a longer lifespan and a greater opportunity to gain from preventative and diseasealtering measures. Contemporary cardiology increasingly prioritizes early intervention as a fundamental component in averting longlasting c omplications, repeated cardiovascular incidents, and untimely disabilities.

Physiological Justification for Prompt Action

In younger individuals, cardiovascular afflictions frequently arise at an initia l, potentially reversible phase. Endothelial dysfunction, mild inflammation, metabo lic irregularities, and immune system imbalances can exist long before any evident structural harm occurs. Initiating therapeutic and preventative actions aimed at thes e mechanisms can decelerate or prevent disease advancement, safeguard vascular h ealth, and lower cumulative cardiovascular hazards over time.

Effects on Future Results

Postponed diagnosis and treatment in younger patients relate to hastened ath erosclerosis, repeated ischemic events, heart failure, and increased risk of mortality later in life. Early action, incorporating lifestyle alterations, medication manageme nt, and addressing psychosocial stressors, has proven effective in diminishing the o ccurrences of significant adverse cardiovascular events. Crucially, averting initial myocardial injury helps sustain functional capacity and decreases the chances of ch ronic disability during the most productive phases of life.

Significance of Preventative and Customized Strategies

Contemporary methodologies emphasize the necessity for tailored risk evalu ations in younger individuals. Proactive screening for genetic susceptibilities, meta bolic issues, and inflammatory indicators facilitates targeted prevention approaches . Lifestyle changes, such as quitting smoking, nutritional adjustments, and increase

d physical activity, are notably effective when introduced early, as habits are more pliable among younger populations.

Economic and Life Quality Considerations

Cardiovascular ailments in younger patients impose considerable economic r epercussions, including decreased productivity, long-
term healthcare expenses, and psychological stress. Proactive measures not only en hance clinical results but also foster improved life quality, social interaction, and m ental health. Preventing disease advancement minimizes the risk of prolonged relia nce on medical care and support systems for disability.

Future Perspectives

Improvements in digital health innovation, imaging methods, and biomarkers are expected to enhance early detection and intervention strategies. Integrating these
instruments into standard clinical procedures may facilitate active management of cardiovascular risks in young individuals before irreversible damage sets in.

Proactive intervention strategies are especially essential for younger patients, as they present a distinctive chance to avert lasting complications and disability. B y tackling harmful mechanisms at early stages and adopting personalized preventiv e measures, it becomes feasible to substantially lessen the impact of cardiovascular conditions and enhance long-term health prospects in this demographic.

Pro-inflammatory cytokines are a broad class of signaling proteins produced by immune and vascular cells, key to regulating the body's inflammatory response. Among the most studied are tumor necrosis factor-α (TNF-α), interleukins IL-1β, IL-6, and IL-8, which participate in the initiation and progression of the atherosclerotic process.

Modern understanding of atherosclerosis considers it as a chronic inflammatory disease of the arterial wall**,** in which local and systemic inflammatory mechanisms determine the stability of plaques, their tendency to rupture, and the development of acute coronary events. Increased levels of pro-inflammatory cytokines are recorded both in the blood plasma of patients with coronary artery disease and in the tissues

of atherosclerotic plaques, reflecting the activity of the immune response and the involvement of macrophages, T-lymphocytes, and endothelial cells.

TNF-α and IL-1β are among the central mediators of inflammation in atherosclerosis. They enhance the expression of adhesion molecules on the endothelium, promote the recruitment of monocytes into the subendothelial space, and stimulate the synthesis of other pro-inflammatory mediators, including IL-6. The activity of these cytokines is linked to an increase in acute inflammation markers and plaque instability, which is associated with a higher risk of developing acute coronary syndromes.

Interleukin-6 (IL-6) is characterized as an important prognostic biomarker in cardiovascular diseases. Its increased concentration is closely associated with the progression of the atherosclerotic process, impaired endothelial function, increased systemic inflammation, and an increased risk of myocardial infarction and heart failure. IL-6 also participates in the regulation of acute phase protein synthesis (e.g., C-reactive protein), influencing the systemic inflammatory response.

IL-8 and other chemokines perform the function of chemoattractors, attracting neutrophils and monocytes to the sites of inflammation, which enhances the formation of an atherosclerotic plaque and increases the risk of its instability. Analysis of IL-8 levels in patients with coronary artery disease shows a significant increase compared to the control, which indicates a close relationship between this cytokine and the immuno-inflammatory nature of the disease.

The molecular mechanisms of action of pro-inflammatory cytokines include the activation of key intracellular signaling pathways, such as NF-κB, which leads to the expression of genes responsible for the further production of inflammatory mediators and the remodeling of the vascular wall. These processes contribute to increased endothelial permeability, increased cellular adhesion, and the migration of monocytes into the arterial intima - mandatory stages of atherogenesis.

In recent years, the role of additional pro-inflammatory mediators (e.g., IL-18) has been actively studied, which are also involved in inflammation, plaque

instability, and atherosclerotic formation rupture processes, offering new perspectives for prognostic models and therapeutic interventions.

Thus, the literature confirms that the imbalance between pro- and anti-inflammatory cytokines underlies the progression of the atherosclerotic process and is associated with an unfavorable clinical outcome. Quantitative determination of these mediators in clinical studies is considered an important marker of inflammatory activity and a potential target for therapeutic strategies.

Cytokines are low molecular weight proteins that perform the function of biologically active mediators of cellular signaling, regulating immune and inflammatory processes. Under normal conditions, the balance between pro- and anti-inflammatory cytokines ensures an adequate immune response without excessive inflammation. Disruption of this balance plays a key role in the pathogenesis of chronic inflammatory diseases, including atherosclerosis and coronary heart disease (Chen et al., 2021).

Anti-inflammatory cytokines (e.g., IL-10, IL-4, TGF-β) participate in the regulation of the inflammatory response, suppressing the synthesis and action of pro-inflammatory mediators, modulating the activity of immune cells, and improving the state of the vascular endothelium. Their study is important for developing strategies for the prevention and treatment of cardiovascular diseases (Kumar et al., 2022).

IL-10 is one of the most studied anti-inflammatory cytokines. It is produced by monocytes, macrophages, regulatory T-cells, and B-cells. Its main mechanisms of action include suppression of pro-inflammatory cytokine expression (TNF-α, IL-1β, IL-6), inhibition of NF-κB activity, and reduction of adhesion molecule expression in endothelial cells (Moore et al., 2020).

In the context of atherosclerosis, IL-10 reduces plaque formation, decreases macrophage activation, and contributes to the stabilization of atherosclerotic foci. It activates the STAT3 signaling pathway, which leads to a decrease in the transcription of inflammatory genes. Clinical studies have shown that low levels of

IL-10 are associated with an increased risk of heart disease progression and an unfavorable prognosis (Zhou et al., 2019).

IL-10 gene polymorphisms are also considered potential risk markers for cardiovascular events. Patients with certain allelic variants of IL-10 have an increased predisposition to the development of atherosclerosis and myocardial infarction (Li et al., 2021).

IL-4 is produced by Th2 cells, mast cells, and eosinophils. It regulates the Th2 type immune response and modulates macrophage activity, promoting the M2 phenotype ("reparative macrophages"), which reduces inflammation and stimulates tissue regeneration (Yang et al., 2020).

IL-4 inhibits the production of TNF-α and IL-1β, reduces the sensitivity of endothelial cells to pro-inflammatory signals, and promotes vascular function. In studies on animal models, IL-4 demonstrated its ability to slow the progression of atherosclerotic lesions, improve endothelial function, and reduce inflammatory activity in the vascular wall (Smith et al., 2021).

Other cytokines, such as IL-13 and TGF-β, also have anti-inflammatory activity, participating in the regulation of the immune response and the resolution of inflammatory processes (Kang et al., 2019).

Anti-inflammatory cytokines are considered potential biomarkers and therapeutic targets for cardiovascular diseases. Measuring the levels of IL-10 and IL-4 allows for assessing the degree of inflammation and the prognosis of clinical outcomes in patients with coronary artery disease (Moore et al., 2020).

Modern research is aimed at developing strategies that increase the activity of IL-10 and IL-4 or stimulate their receptors, which can potentially reduce the progression of atherosclerosis, reduce endothelial dysfunction, and improve the prognosis in patients with high cardiovascular risk (Zhou et al., 2019).

Anti-inflammatory cytokines play a key role in regulating the immune response in chronic inflammatory processes, including coronary heart disease. IL-10 and IL-4 contribute to the limitation of pathological inflammation, stabilization of atherosclerotic plaques, and preservation of endothelial homeostasis. Their

functional activity and genetic variations influence the risk of cardiovascular diseases and can serve as prognostic markers and therapeutic targets.

Thus, the study of anti-inflammatory cytokines opens up prospects for developing personalized therapeutic strategies aimed at reducing cardiovascular risk and improving patient prognosis.

Innovative approach to the therapy of patients with coronary artery disease in young patients

Every year, more than 17 million people worldwide die from cardiovascular diseases, with more than half of the deaths caused by coronary heart disease (CHD). Young adults represent the main labor and production resource of society, determining its socio-economic development. In the context of the trend towards rejuvenation of the age category of patients with high mortality, identifying the features of the clinical course of the disease and identifying risk factors (RF), as well as developing strategies for their correction in young patients, is a priority task for healthcare.

The main risk factors for atherosclerosis and its complications are dyslipidemia and cytokine imbalance. These processes cannot be considered separately, as their combination significantly increases the likelihood of disease progression. Based on the assessment of RF, therapeutic approaches are formed, including both non-drug and pharmacological treatment methods for patients with coronary artery disease. Currently, the therapy of young patients with coronary heart disease against the background of dyslipidemia and cytokine imbalance using drugs that affect lipid metabolism and inflammatory processes remains relevant. Despite the expansion of the range of medications, choosing the optimal therapy for a specific patient remains a complex task of clinical practice.

The goal of treating patients with coronary artery disease is to improve the quality of life, reduce the frequency of anginal attacks, prevent myocardial infarction, and improve survival rates, which corresponds to modern evidence-based medicine recommendations. In addition to lifestyle modifications, treatment

includes medication therapy: prolonged action nitrates, β-blockers or calcium channel blockers, antiplatelet agents (acetylsalicylic acid, clopidogrel), and statins. Despite the achievements in interventional methods of treating coronary artery disease (angioplasty, stenting, coronary artery bypass grafting), optimizing drug therapy remains a pressing issue.

Of particular interest is the combined drug of domestic production ("Temur Med Farm" LLC, Tashkent) - levocarnitine + L-arginine hydrochloride, which includes the amino acids levocarnitine and arginine.

Levocarnitine ensures the transport of fatty acids in mitochondria, supporting β-oxidation and ATP synthesis. In patients with coronary heart disease, chronic heart failure, dyslipidemia, and diabetes mellitus, levocarnitine deficiency is often observed. Its therapeutic effect manifests itself in the stimulation of aerobic glycolysis, improvement of coronary blood flow, antioxidant and antiarrhythmic effects. Levocarnitine also promotes fat depot mobilization, participates in the breakdown of long-chain fatty acids with the formation of acetyl-CoA and ketone bodies, optimizes oxidative phosphorylation and ATP synthesis processes, and reduces the toxic effects of accumulated acetyl-CoA on myocytes and coronary artery endothelium.

The bioavailability of levocarnitine is ensured by its endogenous synthesis (in the liver and kidneys) and intake with food. Endogenous synthesis depends on lysine and methionine, vitamins C, B6, niacin, and iron ions. Levocarnitine regulates the rate of oxidation of long-chain fatty acids and reduces systemic oxidative stress, which is important for the complex therapy of coronary heart disease and post-infarction cardiosclerosis.

As part of the drug, L-arginine is a donor of nitrogen oxide (NO), contributing to the dilation of coronary vessels, improving collateral blood flow, reducing the frequency of angina attacks, and reducing the need for nitrates. It has antioxidant, cytoprotective, and membrane-stabilizing properties, reduces platelet aggregation and leukocyte activation, participates in fibrinolysis processes, and maintains the body's energy supply.

Research data show that the combination of levokarnitin and L-arginine contributes to improved myocardial metabolism, increased duration of physical activity, reduction of ischemic damage and necrosis zones, and improvement of the quality of life of patients with coronary heart disease.

While established treatment methods are generally effective, they may not fully address the specific requirements of this younger demographic. Contemporary cardiology is increasingly exploring groundbreaking therapeutic avenues designed for early disease modification, customized care, and the prevention of future complications.

Tailored and Precise Medical Care

A particularly promising development in treating CAD in young patients is the implementation of personalized medicine. Genetic analysis and polygenic risk assessment enable the identification of individuals highly susceptible to premature CAD. This facilitates the development of bespoke lipid-lowering regimens, individualized antithrombotic protocols, and the prompt initiation of preventative measures. Precision medicine also contributes to more accurate risk stratification and optimized treatment plans.

Advanced Pharmaceutical Interventions

Innovative pharmacological approaches extend beyond conventional statin-based therapies. Newer agents for lowering lipids, such as PCSK9 inhibitors and RNA-based treatments, offer effective solutions for young patients grappling with severe dyslipidemia or inherited hypercholesterolemia. Anti-inflammatory treatments that target specific inflammatory pathways are emerging as potential disease-modifying options, especially for patients exhibiting signs of immune-driven atherosclerosis.

Interventional and Minimally Invasive Procedures

Progress in interventional cardiology has significantly improved outcomes for young patients requiring revascularization. Drug-eluting stents with enhanced biocompatibility, bioresorbable vascular scaffolds, and advanced intravascular imaging techniques allow for more accurate and lasting interventions. These

innovations aim to reduce the recurrence of narrowing, preserve the integrity of blood vessels, and minimize long-term issues associated with permanent implants.

Digital Health and Remote Monitoring Solutions

Digital health technologies are playing an increasingly vital role in managing CAD in younger patients. Mobile health applications, wearable devices, and telehealth platforms support continuous tracking of physical activity levels, heart rate, blood pressure, and adherence to treatment. These tools enhance patient engagement, encourage beneficial lifestyle changes, and enable the early detection of disease progression or treatment-related concerns.

Lifestyle and Behavioral Innovations

Novel therapeutic strategies also emphasize structured interventions related to lifestyle and behavior. Programs that integrate behavioral psychology, stress management techniques, and digital coaching have demonstrated improved adherence to healthy habits.

Regenerative Medicine and Cell-Based Therapies

Regenerative medicine presents groundbreaking strategies for repairing damaged heart muscle and enhancing blood vessel function. Investigations into stem cells, specifically mesenchymal stem cells and induced pluripotent stem cells, indicate promise for fostering new blood vessel growth, diminishing scar tissue formation, and boosting the heart's pumping efficiency. These techniques hold particular relevance for younger individuals, whose inherent capacity for regeneration is greater, potentially leading to more enduring and sustained benefits.

Gene-Based Interventions

Gene therapy constitutes another frontier, focused on rectifying genetic anomalies that underpin certain early-onset forms of coronary artery disease (CAD), or on stimulating the production of therapeutic proteins. For instance, introducing genes that code for vascular growth factors can stimulate angiogenesis and improve blood flow to oxygen-deprived regions. While this domain is still in its nascent stages of clinical evaluation, it holds the potential to fundamentally alter how hereditary CAD is managed and to improve outcomes for younger patients.

Artificial Intelligence and Machine Learning Applications

The deployment of artificial intelligence (AI) and machine learning (ML) is revolutionizing the identification, risk assessment, and treatment planning for CAD in younger demographics. AI algorithms are capable of processing extensive clinical datasets, imaging results, and genetic information to reveal subtle patterns, forecast future adverse events, and refine personalized therapeutic regimens. This facilitates more precise patient categorization, prediction of treatment efficacy, and customization of interventions, which is especially valuable within the intricate and diverse population of young patients.

Integrated Strategies and Comprehensive Patient Care

Beyond advanced technological methods, there is a growing emphasis on integrated approaches that merge conventional medical practices with complementary and alternative therapies.

Concluding Remarks

Innovative approaches to managing CAD in young patients represent a multifaceted strategy encompassing genetic insights, pharmacological interventions, procedural techniques, digital technologies, and regenerative medicine. Ongoing research and collaborative efforts across disciplines will continue to shape the trajectory of cardiology, delivering increasingly effective and tailored solutions.

CHAPTER 2.
Clinical features of the manifestation of coronary heart disease in young people, stratification of risk factors

Clinical features of the manifestation of coronary heart disease in young people

The clinical manifestation of coronary heart disease in young patients has a number of features. Young people are significantly less likely to seek medical attention for chest pain than people in older age groups. Moreover, the history and characteristics of pain syndrome in this category of patients often do not indicate ischemic myocardial damage, which reduces the informativeness of classical symptoms for diagnosis. Before the onset of anginal attacks in young patients, a short ischemic history is observed, and according to foreign studies, only about 24% of such patients seek medical attention due to pronounced angina attacks, while 69% of patients had an unprecedented history of anginal pain before the onset of coronary artery disease.

One of the first systematic studies of the etiology and clinical course of coronary artery disease in young patients was the work of D. M. Aronov (1968), which included 325 patients under 39 years of age. In the study, 34% of patients had coronary insufficiency without focal myocardial damage, 21% had acute myocardial infarction (AMI), and 45% had post-infarction cardiosclerosis (PICS). Diagnosis verification in some patients was performed using coronary angiography. The main cause of coronary heart disease in young patients was CA atherosclerosis, which was

detected in 89% of patients. Atherosclerosis in the absence of CA is present in about 20% of cases, congenital anomalies of CA - about 4%.

The most significant anatomical anomalies of the CA include: the departure of the CA from the pulmonary artery, anomalies in the departure of the left CA trunk or anterior interventricular branch from the right Valsalva sinus, the right CA from the left Valsalva sinus, as well as the intracardial course of the CA. Clinical manifestations of these abnormalities may include chest pain, syncopal states, especially during physical exertion, and the first manifestation can sometimes be sudden cardiac death. In the register of sudden death in 286 athletes under 35 years of age, CA anomalies were detected in 13% of cases, falling behind only hypertrophic cardiomyopathy in frequency.

Embolic events are also a cause of coronary artery disease in young patients, accounting for about 5% of MI cases. These include: thromboembolism in non-compact left ventricular myocardium with pronounced trabecularity and deep intertrabecular spaces, paradoxical thromboembolism through an open oval window, as well as embolism in endocarditis and cardiac tumors (myxoma, papillary fibroelastoma).

For the diagnosis of atherosclerosis, biochemical markers and instrumental methods are widely used, however, their use is limited by the high lability of indicators, low specificity, late penetration, and pronounced dependence on external factors.

Prognostic assessment is a key element in managing patients with coronary heart disease, allowing doctors to choose the optimal treatment tactics. Searching for factors influencing the prognosis, as well as developing methods to influence them, especially in patients who cannot undergo revascularization, remains a pressing task. At the same time, individuals under 45 years old are underrepresented in studies, despite the increase in their proportion in the population, and data on the prevalence of cardiovascular diseases among the working-age population are extremely limited.

Coronary heart disease (CHD) in younger demographics presents a unique medical puzzle due to its unusual symptomology, delayed identification, and

substantial long-term ramifications. While CHD is typically linked with advanced age, its occurrence in younger individuals—generally defined as those under 45—has garnered increasing scrutiny. A thorough understanding of CHD's clinical characteristics in this cohort is crucial for prompt recognition, timely intervention, and improved patient outcomes.

Coronary heart disease (CHD) has historically been viewed as a condition primarily affecting individuals in their middle and later years. However, current epidemiological data reveal a growing occurrence of CHD among younger adults (under 45 years old). Prompt diagnosis and thorough risk assessment are crucial for averting severe complications, such as heart attacks and sudden cardiac arrest.

Manifestations

CHD in younger individuals can present differently compared to older population

Unusual Angina:

- Pain might be vague, radiating to the back, neck, or upper abdomen.
- Often provoked by emotional strain or physical exertion.
- **Myocardial Infarction (MI):**
- In younger adults, MI is more frequently caused by coronary thrombosis with minimal arterial plaque buildup.
- Symptoms can include heart palpitations, sweating, tiredness, or shortness of breath, without the typical severe chest pain.
- **Arrhythmias and Sudden Cardiac Death:**
- The risk is elevated in cases involving congenital coronary abnormalities, long QT syndrome, or inherited predispositions.
- **Asymptomatic Disease:**
- CHD may show no symptoms and only be discovered through stress tests or as incidental findings during evaluations for other health issues.

Predisposing Factors

Younger adults often exhibit a combination of established and age-specific risk factors:

- **Traditional Risk Factors:**

- Hyperlipidemia (elevated LDL cholesterol)
- High blood pressure
- Smoking
- Obesity, especially central adiposity
- Diabetes

- **Age-Specific Risk Factors:**

- Family history of premature CHD
- Psychological stress, depression, chronic fatigue
- Alcohol or substance misuse
- Hypertriglyceridemia, metabolic syndrome
- Inflammatory or autoimmune conditions

Risk Assessment

Evaluating CHD risk in younger adults involves multiple strategies:

- **Clinical Scoring Systems:**

- Tools like the Framingham Risk Score or SCORE are less accurate for individuals under 40 and may require adjustments.

- **Laboratory and Imaging Techniques:**

- Lipid profile, blood glucose, inflammatory markers (CRP, homocysteine)
- ECG, stress echocardiography, or coronary CT angiography to detect early atherosclerosis.

- **Genetic Screening:**

- Variations in genes affecting lipid metabolism, blood clotting, or vascular reactivity can indicate high risk in younger adults.

Prevention and Clinical Implications

- **Lifestyle Modifications:** Quitting smoking, weight management, regular physical activity.
- **Pharmacological Interventions:** Statins or antihypertensive medications when appropriate.
- **Early Detection:** Especially for individuals with a family history of early-onset CHD.

CHD in younger adults demands heightened clinical vigilance, as its presentation can be atypical, and conventional risk scores might underestimate the true risk. Comprehensive risk stratification—incorporating genetic, biochemical, and imaging data—enables the identification of high-risk individuals and reduces the likelihood of early cardiovascular events.

Symptomatology and Clinical Presentation

The way CHD manifests in young people often diverges from its presentation in older patients. While classic chest pain (angina pectoris) remains a frequent complaint, younger individuals more commonly experience atypical or less specific indicators. These might include unusual chest discomfort, pain in the upper abdomen, breathlessness, fatigue, heart palpitations, or fainting spells. Such vague symptoms can lead to misinterpretation or an underestimation of cardiac risk.

Acute coronary syndrome frequently serves as the initial clinical sign of CHD in young individuals, sometimes appearing without any prior warning. In certain instances, sudden cardiac death can be the first manifestation, underscoring the silent yet aggressive nature of this condition in this age group.

Gender-Related Differences. The clinical features of CHD in young people exhibit notable distinctions based on gender. Young men more often present with typical ischemic chest pain, whereas young women frequently report atypical symptoms like shortness of breath, nausea, or back pain. Hormonal influences, microvascular dysfunction, and variations in plaque structure contribute to these differences and can impede diagnosis in female patients.

Disease Severity and Coronary Anatomy

Young patients with CHD often display less extensive involvement of the coronary arteries, frequently characterized by disease in a single vessel. However, despite a lower overall burden of atherosclerosis, plaques in young individuals tend to be more fragile and prone to rupture. Non-atherosclerotic mechanisms, such as coronary artery spasm, spontaneous coronary artery dissection, or thrombosis, can play a significant role in how the disease presents.

Diagnostic Challenges

The unconventional clinical presentation of CHD in young people creates diagnostic hurdles. Low clinical suspicion, the absence of traditional risk factors, and normal findings from initial tests can delay diagnosis. Advanced diagnostic tools, including highly sensitive cardiac biomarkers, coronary computed tomography angiography, and intravascular imaging, have enhanced the detection of early and non-obstructive disease in this population.

Psychosocial Impact

Timely identification and correction of risk factors in young patients with coronary heart disease will reduce both mortality and loss of working capacity, which justifies the relevance of this dissertation work. The use of modern literature data in clinical practice contributes to the early detection of high-risk groups, improvement of diagnosis, therapy, and prognosis of cardiovascular complications.

CHAPTER 3.
Results of domestic and foreign research on the occurrence of risk factors in patients with unstable angina variants in young men

Despite significant achievements in the diagnosis, treatment, and prevention of coronary heart disease (CHD), this disease remains one of the key problems in modern cardiology and healthcare in general. The main reason for hospitalization of patients with coronary artery disease is the development of acute coronary syndrome (ACS). After confirming the diagnosis, one of the primary tasks is to assess the patient's prognosis. Stratification of the risk of complications in coronary artery disease is necessary for choosing optimal management tactics, determining hospitalization periods, and developing individual rehabilitation and secondary prevention programs.

Patients with coronary artery disease have an increased risk of adverse cardiovascular events, including acute myocardial infarction (AMI), stroke, recurrent angina, and sudden cardiac death, both during their hospitalization and in the long term. At the same time, the existing methods of risk stratification remain imperfect, which requires the search for additional prognostic markers, including laboratory indicators, as well as clarification of the prognostic significance of already known parameters for assessing the probability of adverse outcomes and monitoring the effectiveness of therapy.

To increase the accuracy of risk stratification, the use of biomarkers reflecting various pathophysiological mechanisms of the disease is proposed. Despite the constant improvement of medical care, identifying factors influencing the development of post-hospital complications in patients with coronary artery disease remains a pressing task.

Introduction

Unstable angina stands out as a significant clinical presentation of acute coronary syndrome, and its diagnosis is becoming more frequent in younger male populations. While coronary heart disease has historically been linked to older age demographics, both national and global research points to a rising incidence of unstable angina in men under 45. Grasping the patterns and impact of risk factors within this demographic is crucial for timely detection, proactive prevention, and enhancing long-term health outcomes.

Key Traits of Younger Men Experiencing Unstable Angina

Investigations conducted across various nations reveal that younger men diagnosed with unstable angina often exhibit a distinct set of risk factors when contrasted with their older counterparts. In numerous instances, unstable angina serves as the initial clinical indicator of coronary artery disease for this age group.

Established Cardiovascular Risk Factors

Both domestic and international studies consistently highlight the widespread presence of established cardiovascular risk factors among young men afflicted with unstable angina.

- Smoking emerges as the most prevalent and impactful risk factor, cited in the majority of studies. The rate of current smokers among young men with unstable angina significantly surpasses that of age-matched control groups, underscoring its pivotal role in initiating ischemic events.
- Dyslipidemia, specifically elevated levels of low-density lipoprotein cholesterol and diminished high-density lipoprotein cholesterol, is commonly observed and plays a part in the early development and instability of atherosclerotic plaques.
- Arterial hypertension, though less common than in older individuals, remains a significant contributing factor and is often overlooked or undiagnosed in younger patients.
- Diabetes mellitus and impaired glucose metabolism, while reported less frequently, substantially elevate the risk of unstable angina when present.
- Excess weight and obesity, coupled with a sedentary lifestyle, are increasingly prevalent and are associated with detrimental metabolic and inflammatory profiles.

Family History and Genetic Susceptibility

Both national and international research underscores the importance of a family history of early-onset coronary artery disease in young men experiencing unstable angina. Genetic predisposition plays a vital role in accelerating the atherosclerotic process and increasing the vulnerability of plaques. Certain studies suggest a link between unstable angina and genetic variations affecting lipid metabolism, inflammation, and blood clotting mechanisms.

Psychosocial and Lifestyle Influences

Psychosocial stressors, anxiety, and challenging socioeconomic circumstances are frequently reported among young men with unstable angina. Persistent stress can lead to imbalances in the autonomic nervous system, impaired endothelial function, and a pro-inflammatory state, all of which can precipitate episodes of ischemia. Alcohol misuse and the use of psychoactive substances also contribute to the heightened risk. These factors can exacerbate underlying cardiovascular vulnerabilities and trigger acute coronary events.

Specific Considerations for Young Men

Beyond the general risk factors, certain aspects are particularly relevant to the younger male demographic experiencing unstable angina. The rapid progression of atherosclerosis in this group can be attributed to a combination of genetic susceptibility and exposure to potent environmental triggers like smoking and poor lifestyle choices. Furthermore, the psychological impact of experiencing a serious cardiac event at a young age can be profound, necessitating comprehensive support and rehabilitation strategies.

Diagnostic Challenges and Management Implications

The atypical presentation of symptoms in younger individuals can sometimes lead to delayed diagnosis. Clinicians must maintain a high index of suspicion for unstable angina in young men presenting with chest pain or related symptoms, even in the absence of traditional risk factors. Early and accurate diagnosis is paramount to initiating timely medical management, including antiplatelet therapy, statins, and beta-blockers, to stabilize the coronary plaque and prevent further ischemic events.

Future Directions and Research Needs

Continued research is essential to further elucidate the specific pathophysiological mechanisms underlying unstable angina in young men. Identifying novel genetic markers and understanding the interplay between lifestyle, psychosocial factors, and cardiovascular health in this population will be crucial for developing targeted prevention strategies. Furthermore, long-term follow-up studies are needed to assess the effectiveness of current management approaches and to identify optimal strategies for secondary prevention in this unique patient group. The focus should be on promoting healthy lifestyle choices from an early age and addressing modifiable risk factors proactively to mitigate the growing burden of premature coronary artery disease.

Clinical characteristics of patients

The study included 110 patients diagnosed with coronary heart disease (CHD) who were treated in the Emergency Therapy Department No. 2 of the Samarkand branch of the Republican Scientific Center for Emergency Medical Care (RSCEMC SF) and in the CHD departments of the Samarkand Regional Branch of the Republican Specialized Scientific and Practical Medical Center of Cardiology (RSNPMCC SRF). The age of the patients ranged from 22 to 44 years.

To analyze gender differences, patients were divided into two groups: the first group included 65 men with an average age of 39.6±5.1 years, the second group included 45 women with an average age of 38.5±4.6 years. The control group consisted of 86 practically healthy individuals comparable in age and gender to the examined patients (see Figure 2.1).

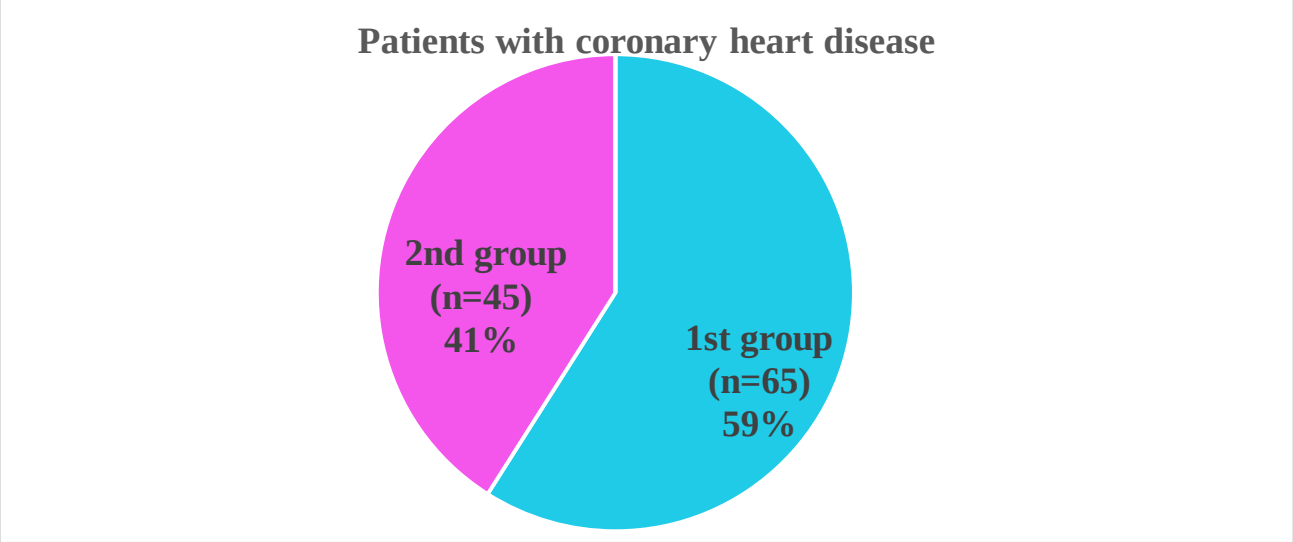

Fig. 2.1. Distribution of patients by sex.

Inclusion criteria: patients with coronary artery disease aged 22 to 44 years.

Exclusion criteria included:

- patients aged 18-44 years, in whom the diagnosis of coronary heart disease has not been confirmed;
- individuals with severe comorbidities, such as acute cerebrovascular disorders, acute or chronic diseases in the acute phase;
- patients with hemodynamically significant heart defects;
- individuals with mental illnesses or a history of craniocerebral injuries.

When distributing patients by age categories, the World Health Organization (WHO, 2023) classification was used, including: young age (18-44 years), middle age (45-59 years), elderly age (60-74 years), senile age (75-89 years) and long-livers (over 90 years).

The severity of unstable angina was assessed using Brownwald's modified classification (2000), which provides for the following variants: first-time angina (VVS), progressive angina of tension (PSN), variant (Prinzmetal) angina, early post-infarction angina.

All patients underwent a comprehensive examination, including: general clinical examination, electrocardiography (ECG), echocardiography (ECHO-CG). ECG monitoring was carried out daily, echocardiography - on the 1st and 8th day of

stay. Laboratory studies were performed on the 1st, 3rd, and 8th day of stay in the department.

When collecting anamnestic data in men with coronary artery disease, the presence of disease symptoms (unstable angina or resting angina, past MI), risk factors (smoking, complicated heredity, hypodynamia, stress, arterial hypertension, diabetes mellitus, obesity, consumption of energy drinks, unbalanced nutrition, etc.) and comorbidities contributing to the severe course of the disease were noted.

Physical examination was conducted according to the standard methodology, with mandatory measurement of blood pressure (BP) and heart rate (HR). Blood pressure measurement was performed according to N.S. Korotkov's method in a sitting position after a five-minute rest.

When assessing anthropometric indicators, height and body weight were recorded, and body mass index (BMI) was calculated using Broca's formula recommended by WHO (1995):

Normal BMI values are 20-25 kg/m2, excess body weight - 25.1-30 kg/m2, obesity of the I degree - 30-34.9 kg/m2, II degree - 35-39.9 kg/m2, III degree - ≥40 kg/m2.

During the examination, the following clinical, anamnestic, and hemodynamic features were identified: practically all patients had 1-3 comorbidities. Arterial hypertension (AH) was diagnosed in 15 (23.1%) men of the 1st group and in 12 (26.7%) women of the 2nd group ($p<0.001$*). Diabetes mellitus was observed in 8 (12.3%) men and 10 (22.2%) women ($p=0.07$). Excess body weight or obesity was detected in 14 (21.5%) men and 18 (40%) women ($p<0.001$*). Anemia was registered in 27 (41.5%) men and 36 (57.8%) women ($p=0.24$). Previously experienced acute cerebrovascular accident was observed in 3 (4.6%) men and 1 (2.2%) woman ($p=0.01$*). Post-infarction cardiosclerosis (PICS) was detected in 15 (23.1%) men and 9 (20%) women ($p=0.004$*). Chronic obstructive bronchitis (COPD) in the anamnesis occurred in 5 (7.7%) men and 2 (4.4%) women ($p=0.31$) (Fig. 2.2).

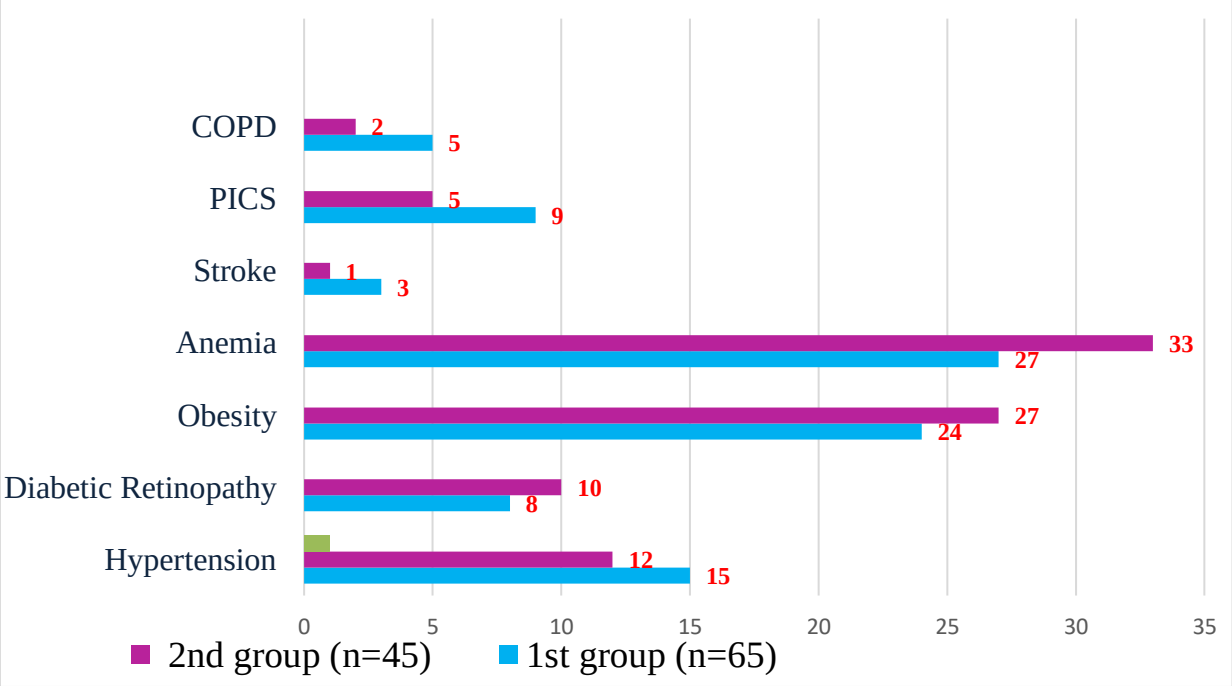

Fig. 2.2. *Frequency of comorbidities in the studied groups*

Drug therapy and clinical examination of patients

On the day of admission, all patients with coronary artery disease underwent standard drug therapy, including:

- β-blockers;
- nitrates;
- anticoagulants and antiplatelet agents (aspirin, klopidogrel);
- statins;
- angiotensin-converting enzyme (ACE) inhibitors.

This treatment continued in the dynamics of patients' stay in the hospital.

Additionally, a comparative analysis of the influence of the Tivorel cardioprotector in combination with traditional therapy on the clinical course of coronary heart disease was conducted.

Clinical, anamnestic, and physical examination of patients was conducted for the purpose of:

- exclusion of extracardiac causes of pain in the pericardial region;
- detection of non-coronary heart diseases;
- determination of extracardiac factors contributing to myocardial ischemia (hypotension, hyperthermia, anemia, etc.);

- identification of cardiac causes that enhance or contribute to myocardial ischemia.

Clinical characteristics of the control group

The control group included 86 practically healthy volunteers aged 22-44 years, with an average age of 37.6±5.3 years.

The average body mass index (BMI) was 24.6±3.08 kg/m2. Distribution by body weight categories:

- normal body weight - 42 people (38.2%);
- excess body weight - 32 people (29.1%);
- obesity of the 1st degree - 12 people (10.9%).

The study of risk factors showed:

- the presence of obesity and early signs of cardiovascular diseases (CVD) in 33 men (30%);
- smoking was observed in 38 people (34.5%), with an average smoking index of 0.33;
- stressful states - in 30 people (27.3%);
- alcohol consumption - 24 people (21.8%);
- energy drinks - 11 people (10%).

Table 2.2

General characteristics of the individuals in the control group

Name of indicators	**Control group (n=110)**
BMI, kg/m^2	24.6±3.08
Normal body weight, kg/m^2	42 (38.2%)
Excess body weight, kg/m^2	32 (29.1%)
I-degree obesity	12 (10.9%)
Weighted heredity	33 (30%)
Smoking	38 (34.5%)
Smoking index	0.33
Stress	30 (27.3%)
Alcohol consumption	24 (21.8%)
Consumption of energy drinks	11 (10%)

2. Research methods

All patients with unstable angina at the time of admission underwent a comprehensive clinical, laboratory, and instrumental examination within the first 24-48 hours, including the following stages:

1. General clinical examination: collection of complaints, anamnestic data, physical and anthropometric examination (height, body weight, calculation of body mass index).

2. Laboratory tests: total blood count (TBC), total urine count (UU).

3. Biochemical blood tests: determination of the level of creatinine, urea, residual nitrogen, high and low-density lipoproteins (HDL, LDL), total cholesterol, triglycerides, as well as the level of glucose in patients with diabetes mellitus.

4. Instrumental studies: electrocardiography (ECG), echocardiography (Echo-CG), Holter ECG monitoring.

2.1 Laboratory research methods

Blood collection was performed on an empty stomach, after 12 hours of fasting, from the cubital vein.

- The concentration of total cholesterol (TC) in blood serum was determined by the photocolorimetric method on an automatic biochemical analyzer "Sapfir 400" using enzyme kits.
- The concentration of glucose in venous blood plasma was determined by glucose oxidase method on the same analyzer.
- To verify the diagnosis of "diabetes mellitus," a repeated assessment of the fasting glycemia level was performed the next day. Exceptions were cases of pronounced hyperglycemia with clinically evident signs of acute metabolic decompensation.

2.2 Instrumental research methods

Monitoring of physiological parameters during the first day included: ECG, heart rate (HR), blood pressure (BP), and blood oxygen saturation (SpO2).

Electrocardiography

- The electrodes were installed on the naked body of the patient in the intensive care unit.
- ECG was performed on a 3-channel MAC 600 electrocardiograph (from the "Sonomedika" company).
- The study was performed upon admission, after 12 hours, in the morning of the next day, and then daily.
- Signs of focal changes in the myocardium were assessed: elevation of the ST segment, pathological Q wave, pathological QRS complex, ST segment depression, bundle branch block, rhythm and conduction disorders, as well as signs of atrial and ventricular overload.

Echocardiography

- It was performed on an expert-class "Logiq 9" device (GE, USA) using a matrix single-crystal sectoral phase sensor of 1.7-4.6 MHz (5S-D).
- The study was conducted in M- and B-modes with pulsed and colored doppler.
- The following were determined: interventricular septum thickness (IVT), left ventricular wall thickness (LVSD), final diastolic and systolic dimensions of the left ventricle (CDR, CRF), ejection fraction (EF) according to Simpson and Teicholtz, stroke volume (SV), and left ventricular myocardial mass (LVM) according to the formula R.B. Devereux and N. Reichek.

Clinical and anamnestic characteristics and frequency of risk factors in patients with coronary artery disease and the control group

This study is based on the observation of 110 patients with coronary heart disease (CHD) who received treatment in the emergency therapy and cardiology departments of the Samarkand branch of the Republican Scientific Center for Emergency Medical Care (RSCEMC SF). The patients' ages ranged from 22 to 44 years.

Patients were divided into groups based on gender:

- 1st group - 65 men (59%), average age 39.6 ± 5.1 years;

- 2nd group - 45 women (41%), average age 38.5±4.6 years.

The control group consisted of 86 practically healthy individuals who met the inclusion criteria (see Figure 3.1.1).

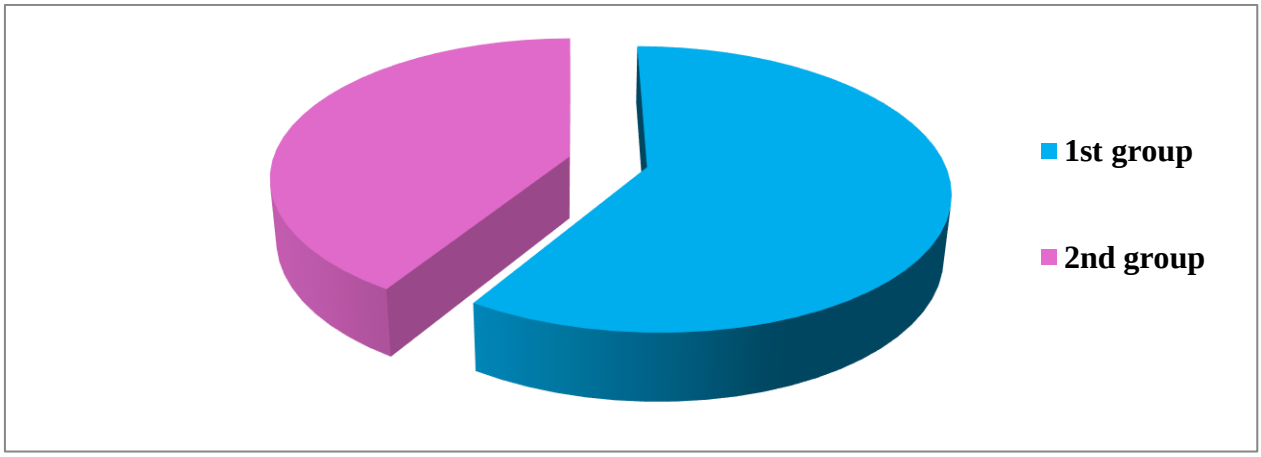

Fig. 3.1.1. Distribution of patients by age groups.

All patients underwent assessment of clinical and anamnestic data, standard general clinical and biochemical studies, including lipid metabolism indicators.

Physical examination was conducted according to standard methodology, with mandatory assessment of weight and height, measurement of blood pressure (BP) and heart rate (HR).

Body Mass Index (BMI) was calculated using Broca's formula recommended by the WHO Committee (1995):

BMI=body mass (kg) height (m) 2.

BMI=height (m) 2body weight (kg)

In normal, BMI is 20-25 kg/m2, excess body weight is determined at BMI 25.1-30 kg/m2, obesity is determined at BMI more than 30 kg/m2. Blood pressure measurement was performed using the N.S. Korotkov method in a sitting position after at least 5 minutes of rest.

When collecting the anamnesis in patients with coronary artery disease, the presence of the disease (early acute myocardial infarction, stress angina or resting), risk factors (atherosclerosis of other vascular areas, arterial hypertension, smoking, diabetes mellitus, obesity, alcohol and energy drinks, improper nutrition), as well as the period preceding the development of unstable angina, and factors contributing to

its occurrence (excessive physical exertion, psycho-emotional stress, hypodynamia, improper lifestyle) were taken into account. Additionally, information was clarified about early manifestations of cardiovascular diseases in close relatives.

Patients were distributed according to the clinical course of coronary artery disease as follows. Among men with coronary artery disease, first-time angina was observed in 35.4% of patients, progressive angina of tension - in 53.8%, and acute myocardial infarction with a Q wave - in 10.8% of patients. Among women, first-time angina was found in 42.2%, progressive angina of tension in 44.4%, and acute myocardial infarction with a Q wave in 13.3% of patients.

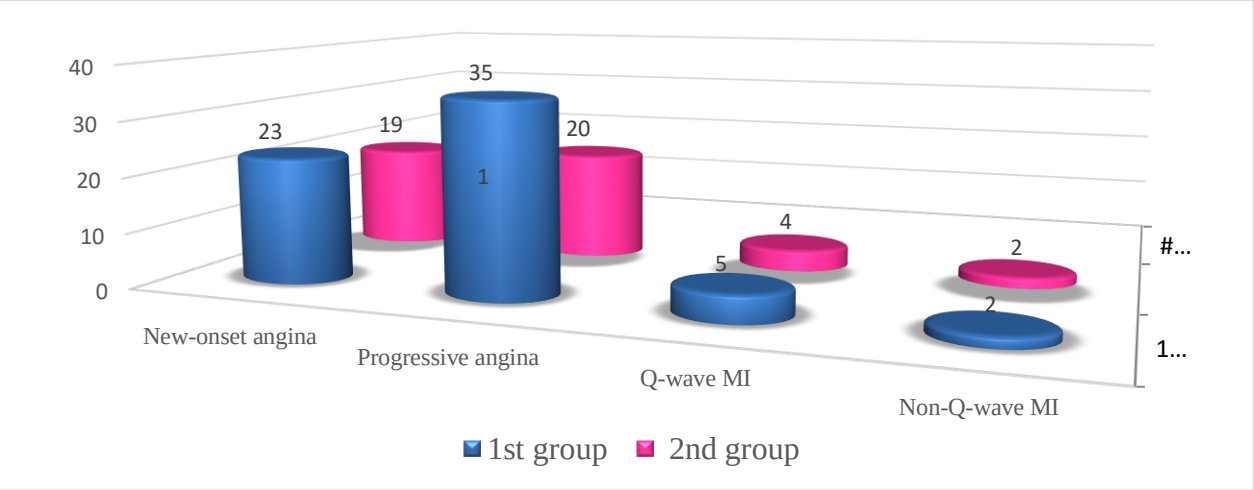

Fig. 3.1.2. Distribution of patients based on the clinical course of coronary artery disease.

When questioning all patients with coronary artery disease, special attention was paid to the main complaint - chest pain. Analysis of the frequency of pain attacks throughout the day showed that in men (1st group), 3-5 attacks per day were observed in 41.5% of patients, while in women (2nd group) this indicator was 31.1% ($p<0.0001$). 6-8 attacks per day were registered in 38.5% of men and 48.9% of women ($p=0.001$). More than 9 attacks per day were observed in 18.5% of men and 14.4% of women, with no statistically significant differences ($p>0.05$).

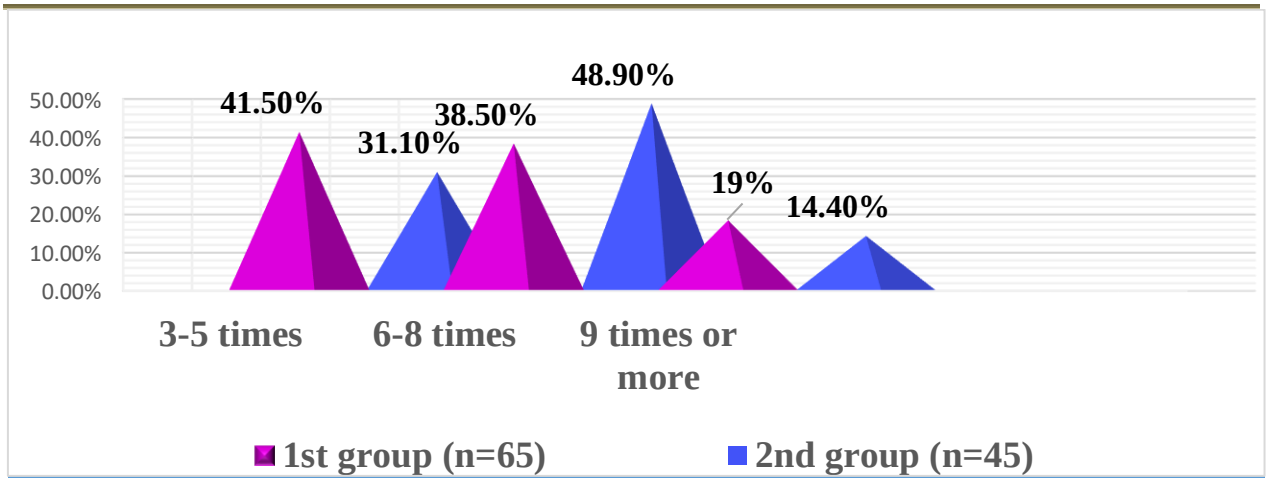

Figure 3.1.3. Distribution of patients by frequency of anginal attacks within a day

When questioning all patients with coronary heart disease, special attention was paid to the time of occurrence of chest pain throughout the day. Analysis showed that angina attacks occurred at night (from 01:00 to 06:00) in 10.8% of men (1st group) and 8.9% of women (2nd group) ($p<0.0001$). Morning attacks (from 06:00 to 12:00) were observed in 27.7% of men and 28.9% of women ($p=0.001$). Daytime attacks (from 12:00 to 18:00) were registered in 36.9% of men and 35.6% of women, with statistically insignificant differences between the groups ($p>0.05$). Evening attacks (from 18:00 to 24:00) occurred in 24.6% of men and 26.7% of women ($p<0.0001$).

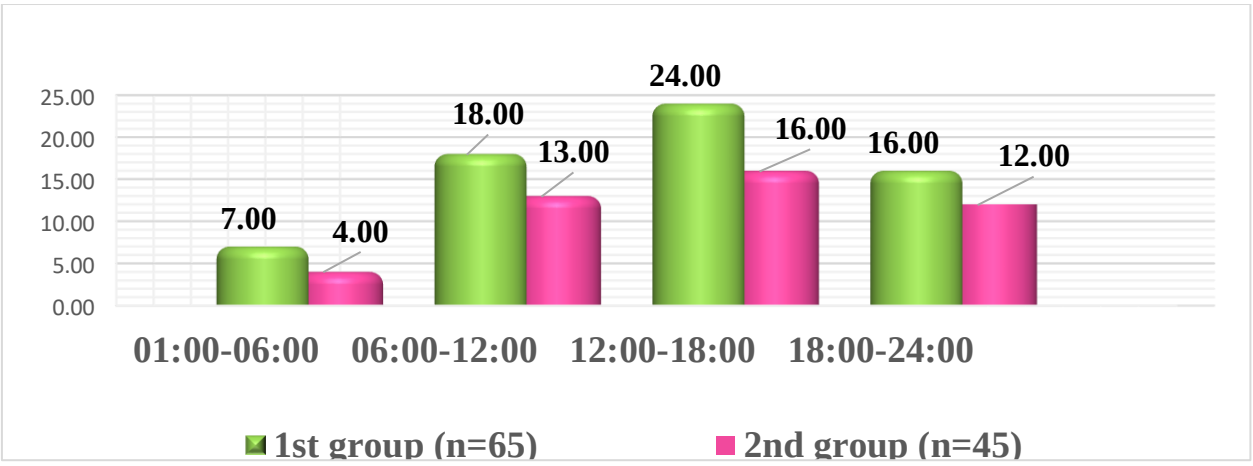

Figure 3.1.4. Distribution of patients by time of occurrence of anginal attacks during the day

When analyzing the occurrence of risk factors (RF) among patients with coronary artery disease, the following indicators were identified. Smoking was one of the most common risk factors and occurred in 56.9% of men (1st group) and 20%

of women (2nd group) (p<0.001). Arterial hypertension (AH) was noted in 27.7% of men and 26.7% of women (p<0.001), diabetes mellitus (DM) - in 7.7% of men and 4.4% of women (p<0.001). Excess body weight or obesity was detected in 21.5% of men and 40% of women (p<0.001). Aggravated heredity for cardiovascular diseases was observed in 24.6% of men and 33.3% of women (p<0.01), while chronic stress was detected in 40% of men and 53.3% of women (p<0.001). Alcohol consumption was noted in 49.2% of men and 11.1% of women (p=0.05).

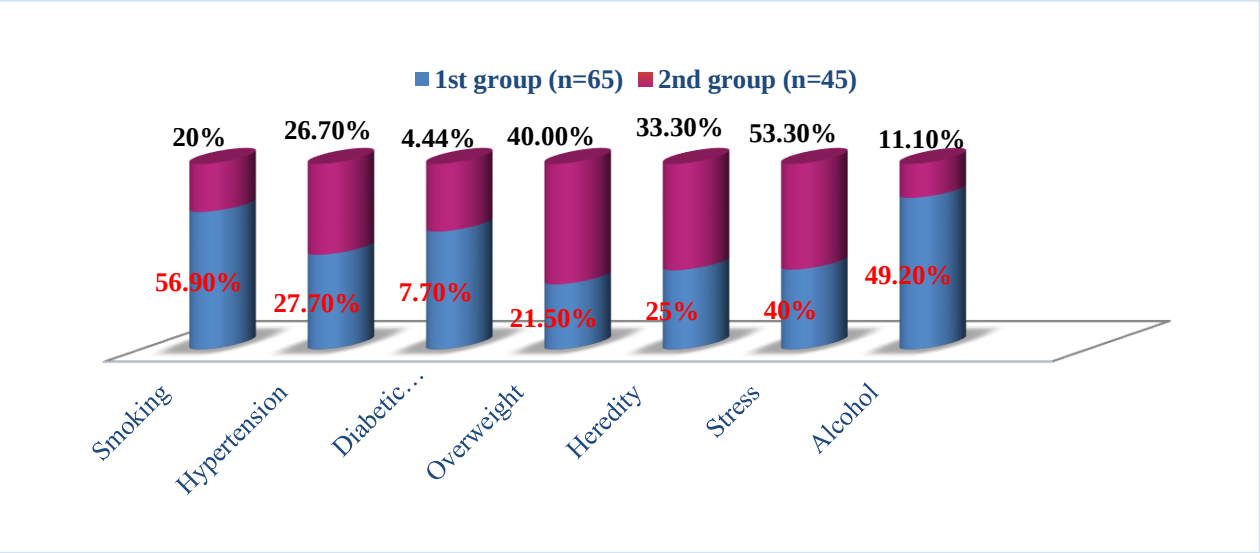

Fig. 3.1.5. Distribution of patients based on the spread of risk factors.

Based on the results of anthropometric examination, the following indicators were identified. The average height of patients in the 1st group was 1.77 m, in the 2nd group - 1.64 m (p=0.0001). The average weight of patients in the first group was 76.7 kg, in the second - 83.2 kg (p=0.05). Body mass index (BMI) was 24.6 kg/m2 in men and 27.7 kg/m2 in women (p=0.01). Among men, normal body weight was observed in 32 (49.2%) patients, among women - in 18 (40%) (p<0.001). Excess body weight was noted in 13 (20%) men and 15 (33.3%) women (p<0.001), obesity of the 1st degree was detected in 1 (1.5%) man and 3 (6.7%) women (p<0.001), (Table 3.1).

Table 3.1.1.

Characterization of patients according to anthropometric data.

Anthropometric indicators	1st group (n=65)	2nd group (n=45)	Mann-Whitney-Wilcoxon-test.
Height (m)	1.77	1.74	0.0001
Weight (kg)	76.7	83.2	<0.001
BMI (kg/m^2)	24.6	27.7	<0.001
Normal mass of a body	32 (49.2%)	18 (40%)	<0.001
Excess body mass	13 (20%)	15 (33.3%)	<0.001
I-degree obesity	1 (1.5%)	3 (6.7%)	<0.001

Thus, the analysis of risk factors in the studied groups showed that male patients with coronary artery disease in most cases have similar risk factors to women with coronary artery disease, which may indicate an increased probability of a more severe course of the disease in the future. Among young patients, smoking, stress, excess body weight or obesity, arterial hypertension, and alcohol consumption are most common, making these factors potentially correctable. The possibility of predicting the risk of developing cardiovascular diseases in young people based on identified risk factors opens up new prospects for developing strategic approaches to the prevention and management of patients with a high risk of adverse outcomes.

3.2. Laboratory test data in young patients with coronary heart disease

Table 3.2.1.

Comparative characteristics of OAQ indicators in patients with coronary artery disease in the general group and depending on gender

Parameter	General sample (n=110)	Men under 45 (n=65) (2)	Women 45 years old (n=45) (3)	*p2-3*
Hemoglobin (g/l)	95.5 (80-110)	100.0 (90-120)	90.1 (75-105).	0.900
Leukocytes, 10^9	10.0 (8.0-12.15)	10.7 (9.0-13.0)	9.85 (8.0-12.0)	0.003
Eosinophils, %	1.0 (0.0-2.0)	0.0 (0.0-2.0)	1.0 (0.0-1.5)	0.943
N/Z neutr,%	1.0 (1.0-3.0)	1.5. (1.0-3.0)	1.0 (1.0-2.0)	0.620

Segm/poison neutr., %	67. (60.0-74.0)	66. 58-73.	68.5 (60-74)	0.238
Total amount of neutrons, %	70. (62.0-76.0)	68. 59-76.	72. (64-76)	0.301
Lymphocytes, %	20.5 (16.0-29.25)	23. (17.0-32.0)	20. (16 - 27.5)	0.556
Monocytes, %	9.0 (6.0-12.0)	10.0 (7.0-13.0)	8.0 (7.0-9.0)	0.025
ESR, mm/h	13.5 (10.0-18.5)	12.0 (9.0-14.0)	15.0 (13.0-18.5)	0.538

Analysis of the general biochemical blood test indicators revealed that glomerular filtration rate (GFR) in women with coronary heart disease was 6.8 ml/min lower than in men, amounting to 92.7±10.5 ml/min versus 99.5±9.5 ml/min in male patients ($p<0.0001$). In the control group, the eGFR averaged 109.8±18.5 ml/min, and the differences with patients with coronary heart disease did not reach statistical significance ($p=0.26$).

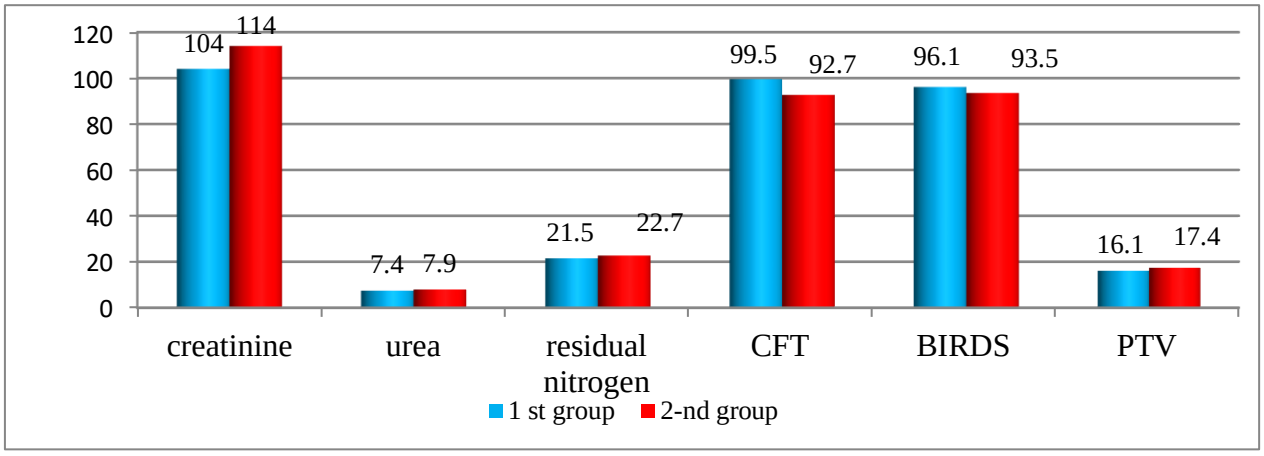

Fig.3.2.1. Blood biochemical analysis indicators in patients with coronary artery disease

Upon examination of the blood lipid spectrum in patients of both groups, an increase in total cholesterol (CH), low-density lipoproteins (LDL), and triglycerides (TG) was noted. Total cholesterol in the 2nd group was 0.26 mmol/l higher compared to the 1st group and amounted to 7.14 mmol/l versus 6.88 mmol/l, respectively ($p=0.049$). Conversely, the level of LDL was higher in the 1st group by

0.37 mmol/l and amounted to 4.50 mmol/l versus 4.13 mmol/l in the 2nd group ($p<0.001$), reflecting lipid metabolism disorders in patients with coronary artery disease. The level of high-density lipoproteins (HDL) practically did not reveal differences between the groups: in the 1st group it was 1.0 mmol/l, in the 2nd - 0.96 mmol/l ($p=0.03$), while the indicators were below the norm in the elderly group. The triglyceride level in the 1st group was significantly higher and amounted to 3.62 mmol/l, and in the 2nd group - 3.19 mmol/l ($p<0.001$). The atherogenicity coefficient (AC) exceeded normal values in both groups and was 5.88 in the 1st group and 6.42 in the 2nd group, while the indicator ≤3.0 ($p=0.03$) is considered normal.

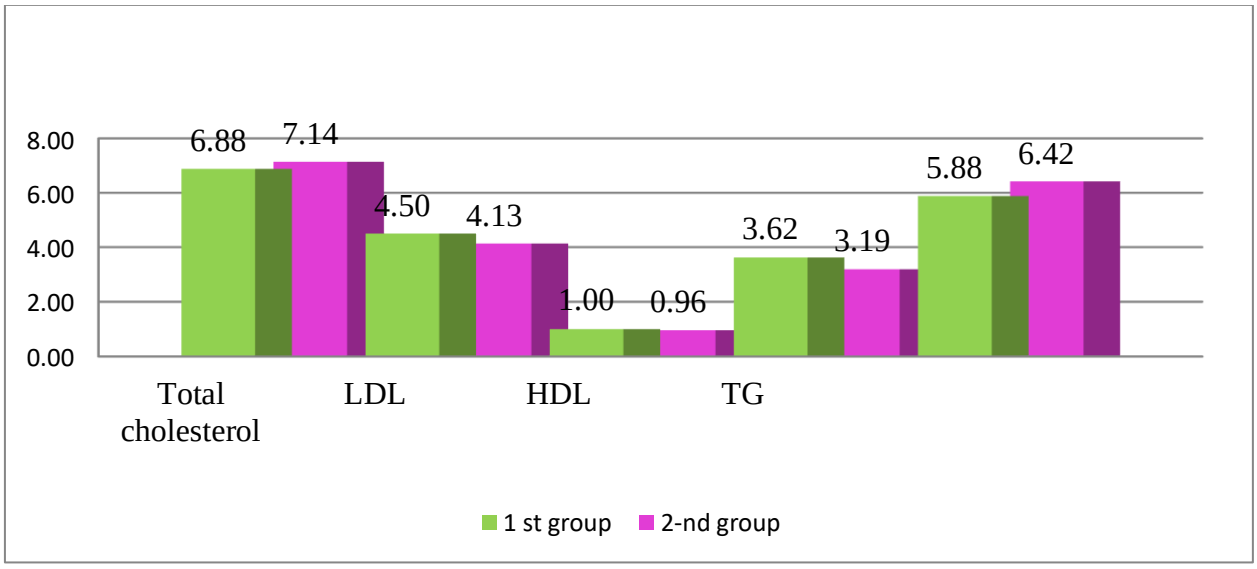

Fig. 3.2.2. Lipid metabolism indicators in patients with coronary heart disease by groups.

Young patients often had comorbidities capable of exacerbating the course of coronary artery disease. Many of them had excess body weight, which was also confirmed by the results of blood lipid analysis. Early detection of risk factors, correction of excess weight, and timely treatment of concomitant pathologies and lipid metabolism disorders in young men contribute to a reduction in the likelihood of cardiovascular complications.

3.3. Indicators of instrumental data in the studied groups electrocardiographic data

Upon admission, all patients underwent an electrocardiographic examination using a Fukuda device, which revealed pathological criteria of unstable angina, such as ST segment elevation or depression, changes in the T wave, appearance of pathological Q waves, regression of the R wave in the V1-V4 leads, rhythm disturbances, and the occurrence of a new complete blockage of the left bundle of Giss.

Analysis of the localization of ischemic changes on the ECG showed the following: anterior wall ischemia was observed in 27 (41.5%) patients of the 1st group and in 15 (33.3%) patients of the 2nd group (p=0.99); posterior wall ischemia of the left ventricle was observed in 26 (40%) patients of the 1st group and in 17 (37.8%) patients of the 2nd group (p=0.45). Ischemic changes in the anterior septal wall were noted in 7 (10.8%) patients of the 1st group and in 7 (15.6%) patients of the 2nd group (p=0.14). Lateral wall ischemia was detected in 5 (7.8%) patients of the 1st group and in 6 (13.3%) patients of the 2nd group (p=0.81). Two or more wall ischemia was registered in 28 (43.1%) patients of the 1st group and in 19 (42.2%) patients of the 2nd group (p=0.79).

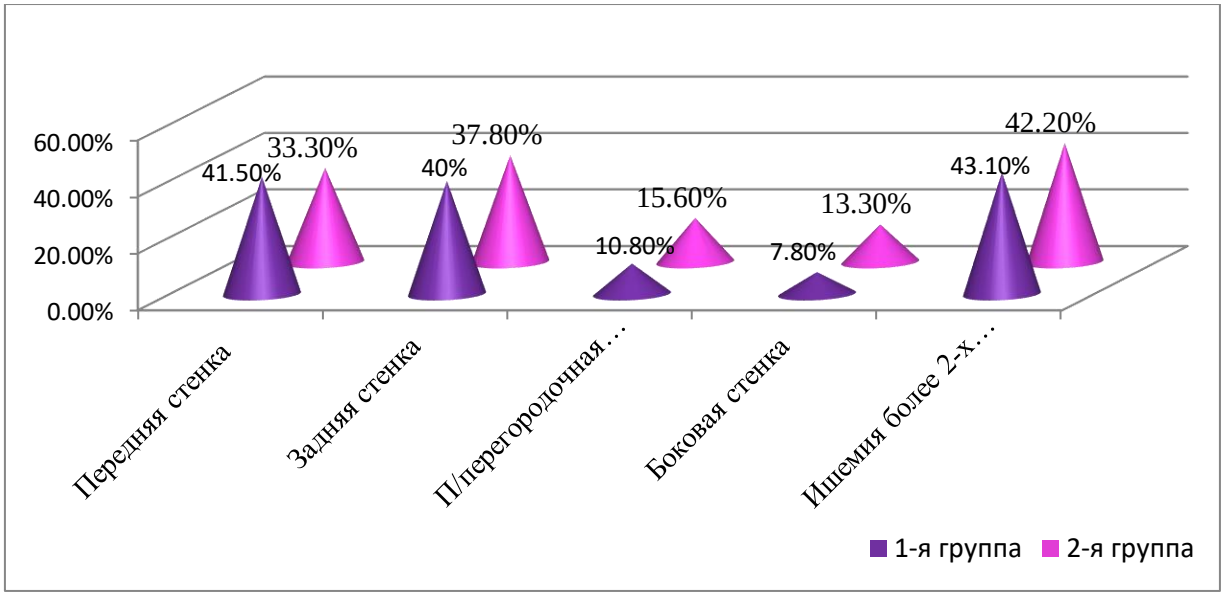

Figure 3.3.1 Distribution in patients with coronary heart disease depending on the ischemic damage to the left ventricle myocardium.

According to ECG data, in young men with coronary heart disease, compared to female patients, the indicators of damage to the anterior and posterior walls were higher and amounted to 41.5% and 40% versus 33.3% and 37.8%, respectively.

Echocardiographic data

According to EchoCG data, the following changes were identified in the studied groups. Left ventricular ejection fraction (LVF) in patients of the 1st group averaged 53.6 ± 8.2%, while in the 2nd group the indicator was lower and amounted to 50 ± 8.4 ($p < 0.01$). In the control group, LVEF was 56% ± 9.0 ($p = 0.48$). The end-diastolic volume (EDV) of the left ventricle in the 1st group reached 140.3±40.0 ml, in the 2nd group - 152±49.0 ml ($p=0.09$), in the control group - 120±20.2 ml ($p<0.05$). The final systolic volume (FSV) of the left ventricle in patients of the 1st group was 78.7 ± 25.2 ml, in the 2nd group - 84.6 ± 36.2 ml ($p = 0.11$), while in the control group it was 56 ± 14.4 ml ($p < 0.001$).

Regarding local contractility disorders, one hypokinesis zone was detected in 30 (46.2%) patients of the 1st group and in 22 (48.9%) patients of the 2nd group ($p = 0.78$). Hypokinesis of more than two zones was noted in 35 (53.8%) patients of the 1st group and in 23 (51.1%) patients of the 2nd group ($p = 0.01$). Akinesis was observed in 24 (36.9%) patients of the 1st group and in 15 (45.5%) patients of the 2nd group ($p = 0.01$). In the control group, the hypo- or akinesis zone was not detected according to EchoCG data.

Table 3.3.1

EchoCG indicators in young patients with coronary heart disease depending on gender and control group.

Indicators EchoCG	1st group	2nd group	Control group
FV (%)	53.6%±8.2	50%±8.4	56%±9.
CDO (ml)	140.3±40	152±49.03	120±20.2
CSF (ml)	78.7±25.2	84.6±36.2	56±14.4
Zone 1 Hypokinesis	30 (46.2%)	22 (48.9%)	0 (0%)
2 or more Hypokinesis	35 (53.8%)	23 (51.1%)	0 (0%)

Akinesis zone	24 (36.9%)	15 (45.5%)	0 (0%)

Thus, according to EchoCG data, ischemic damage to more than two heart walls was more common in young men than in women. The average left ventricular ejection fraction in the 1st group was 53.6%, while in the 2nd group it decreased by 3.6% and amounted to 50%. Hypokinesis of more than two zones was observed in 53.8% of patients in the 1st group, which is 2.7% higher than in patients in the 2nd group (51.1%). At the same time, the akinesia zone was detected in 36.9% of men and 45.5% of women, i.e., it occurred 9% more often in women. These data indicate the severe course of the disease in young patients and emphasize the need for timely and rational therapy, as such changes can lead to early disability and an increased risk of fatal outcome.

CHAPTER 4.
The role of dyslipidemia and pro- and anti-inflammatory cytokines in blood serum in the development of coronary heart disease in young men

Currently, the role of dyslipidemia (DLP) as a risk factor for the development and progression of chronic cardiovascular diseases (CCD), in particular, coronary artery disease (CA) caused by atherosclerotic changes, is considered convincingly proven. Lipid metabolism disorders and lipoprotein levels largely depend on the patient's age, gender, as well as the influence of external factors (nutritional characteristics, composition and quantity of consumed food, physical activity, hypodynamia, dietary regimen) and internal factors (hormonal changes, digestive organ pathology, etc.).

In DLP, lipid metabolism is disrupted in several ways, leading to changes in their concentration in the blood and impaired function. These disorders can be independent, caused by other diseases, or combined with other risk factors contributing to the development of atherosclerosis. Among lipid metabolism disorders, special attention is paid to total cholesterol (TLC), low-density lipoprotein cholesterol (LDL cholesterol), and triglycerides (TG). Numerous randomized studies show that a decrease in the level of CVD and LDL-C leads to a decrease in morbidity and mortality from CSD.

A typical manifestation of LDL is the atherogenic lipid triad: a moderate increase in TG, a decrease in high-density lipoprotein cholesterol (HDL cholesterol), and an increase in the number of small LDL particles. These indicators play an important role in the prevention and treatment of patients with CSD. A decrease in LDL cholesterol levels by 1.0 mmol/l (40 mg/dl) is associated with a 22% decrease in morbidity and mortality from coronary heart disease. Conversely, an increase in LDL-C contributes to the progression of atherosclerotic plaques.

Data from numerous studies also demonstrate a direct relationship between body weight and overall mortality, with mortality being highest at BMI >35 kg/m2. The type of obesity is of particular importance: in the abdominal type, white fat accumulates in the mesentery and omentum, which is an unfavorable predictor of cardiovascular events. The abdominal type of obesity occurs in patients of any age regardless of their total body weight and is considered a modifiable risk factor for coronary artery disease in men. A decrease in LDL-C to 1.4 mmol/l is considered the optimal treatment option.

Atherosclerosis is a chronic inflammatory disease of arteries of medium and large caliber, accompanied by immune disorders in response to endoteliy damage in DLP. The process of atherosclerosis includes several stages: damage to the vascular wall and activation of endothelial cells, transformation of macrophages and monocytes into foamy cells with phagocytosis of oxidized LDL, formation of the fibrous capsule of the atherosclerotic plaque (ASP), migration and proliferation of smooth muscle cells, and ultimately, rupture of the plaque and atherothrombosis.

If previously attention was focused primarily on the lipid theory of atherosclerosis, today great importance is attached to immune-inflammatory mechanisms. Cytokines, low molecular weight histogormonal proteins (5-50 kD), play a key role in the development of aseptic inflammation and the destabilization of ASD.

Among cytokines, pro-inflammatory (IL-1, IL-6, IL-8, IL-12, TNF-α, INF-γ) and anti-inflammatory (IL-4, IL-10) molecules are of particular importance. In atherosclerosis, the balance between pro- and anti-inflammatory cytokines is

disrupted, which contributes to the destabilization of ASD and the progression of IHD. For example, IL-1β enhances the activity of neutrophils and lymphocytes, stimulates the synthesis of acute phase inflammatory proteins, increases the adhesion of leukocytes to the endothelium, and activates the production of IL-6, IL-8, and TNF-α. Conversely, IL-10 blocks the synthesis of pro-inflammatory cytokines and reduces the activity of macrophages, slowing down the damage and thrombosis of ASB.

Analysis of pro- and anti-inflammatory cytokine levels is an important indicator of the clinical course of coronary artery disease, and assessment of cytokine imbalance in combination with markers of ASD damage has practical significance. This emphasizes the need to develop optimal diagnostic algorithms and preventive measures aimed at reducing complications associated with CA atherosclerosis.

Coronary heart disease (CHD) in younger males presents as a distinct clinical condition marked by its early appearance, rapid advancement, and substantial long-term repercussions. Contemporary research emphasizes that the development of CHD in this demographic isn't solely attributable to conventional risk factors. Instead, it arises from intricate interplay between how the body processes lipids and widespread inflammatory responses. Abnormalities in lipid profiles and an imbalance between substances that promote and suppress inflammation in the blood are increasingly recognized as primary drivers of early plaque buildup and instability in young men.

High LDL-C directly harms the inner lining of blood vessels, encourages fat deposits within artery walls, and speeds up the formation of atherosclerotic plaques. Lower HDL-C impairs the body's ability to remove excess cholesterol and reduces its antioxidant defenses, further damaging blood vessels. Genetic predispositions to lipid disorders, such as familial hypercholesterolemia, are particularly noteworthy in younger patients, frequently leading to early-onset CHD even when other risk factors are absent.

The Influence of Pro-Inflammatory Mediators

Inflammation is a crucial factor in the early development of blockages in the heart's arteries in young men. The attraction and activation of immune cells (monocytes and macrophages), which then transform into foam cells.

- Weakening of atherosclerotic plaques, increasing the likelihood of rupture and sudden cardiac events.

Elevated concentrations of these inflammatory substances in the blood have been linked to more severe arterial blockages, even in young men with few traditional cardiovascular risk factors.

The Protective Function of Anti-Inflammatory Mediators

Substances that reduce inflammation, such as IL-10 and TGF-beta, play a vital role in maintaining the health and balance of blood vessels. They help to prevent an overactive immune response, lessen damage to tissues caused by immune cells, and stabilize atherosclerotic plaques. In young men experiencing early CHD, studies frequently reveal lower levels or reduced effectiveness of these anti-inflammatory substances, shifting the balance towards a pro-inflammatory state that accelerates the disease's progression.

The Interconnectedness of Lipid Processing and Inflammation

There's a two-way relationship between abnormal lipid levels and inflammation in the development of CHD:

- Modified LDL cholesterol acts as a powerful trigger for inflammation, activating the cells lining blood vessels and immune system pathways.
- Inflammatory cytokines can promote the uptake of lipids by macrophages, contributing to foam cell formation and plaque development.
- Chronic inflammation can lead to increased hepatic synthesis of triglycerides and reduced HDL-C production, further worsening dyslipidemia.
- This vicious cycle of dyslipidemia and inflammation creates a pro-atherogenic environment that drives the accelerated development of CHD in young men.

Therapeutic Implications

Understanding the intricate interplay between lipid metabolism and inflammation opens avenues for novel therapeutic strategies targeting early CHD in young men.

Beyond aggressive management of traditional risk factors like hypertension and diabetes, interventions aimed at:

- Optimizing lipid profiles: This includes statins for LDL-C reduction, fibrates or niacin for triglyceride management, and potentially novel agents targeting HDL-C or triglyceride-rich lipoproteins.
- Modulating inflammatory pathways: This could involve targeting specific pro-inflammatory cytokines or enhancing the activity of anti-inflammatory mediators. Research into anti-inflammatory drugs and lifestyle interventions that reduce systemic inflammation is ongoing.
- Addressing genetic predispositions: Early identification and management of familial dyslipidemias are crucial.

Coronary heart disease in young men is a complex condition driven by the synergistic effects of dyslipidemia and systemic inflammation. The bidirectional relationship between these two processes creates a potent atherogenic environment, leading to early and aggressive disease progression. A comprehensive approach that addresses both lipid abnormalities and inflammatory pathways is essential for effective prevention and management of CHD in this vulnerable population. Future research should continue to elucidate the precise molecular mechanisms underlying this interaction to develop more targeted and effective therapies.

Method for determining serum lipoprotein concentration blood

Blood lipid profile indicators determined the content of: OXC, LDL, TG, HDL, and atherogenicity coefficient. Lipid determination in the blood was performed using a homogeneous enzymatic colorimetric method on a "Hitachi-902" biochemical analyzer. HDL was determined in the supernatant after the precipitation of lipoproteins of other classes with dextransulfate, LDL concentration was calculated using the Friedwald formula [168]:

LDL=OXC-LDL-TH/5 or LDL (in mmol/l) =OXC-LDL-TH/2.2

There are two assumptions based on this formula: 1) the main part of TG plasma is found in LDL and chylomicrons (CHM); 2) The TG/XC mass ratio in mg in LDL is 5:1, and in mmol is 2.2:1. This formula is not used for high levels of TG>4.5 mmol/l (>400 mg/dl) [38, 107]. Its content in blood serum <180 mg/dl, HDL>40 mg/dl, TG <200 mg/dl was taken as the norm for OXC [38].

The distribution of OX between atherogenic and anti-atherogenic lipoproteins was studied using the atherogenicity coefficient (CoefA) and determined by the following formula:

CoefA= (OXC-LDL) / (DLDL),

where CoefA is the atherogenicity coefficient (in relative units). Normally, the atherogenicity coefficient is within 2-3 IU. If the atherogenicity coefficient is between 3 and 4 units, there is a moderate risk of atherosclerosis development. If the value is greater than 4 units, a high probability of atherosclerosis development is noted. If the value is 7 units or more, this indicates pronounced atherosclerosis.

Method for determining the concentration of cytokines in blood serum

The determination of IL-1β in the blood serum of the examined individuals was carried out by the method of solid-phase enzyme-linked immunosorbent assay (TIFTA) using the "IFA-1IL" set according to the "sandwich" principle, with chernopyl peroxidase as an indicator enzyme. In this method, two epitope-specific monoclonal antibodies to IL-1β were used: one immobilized on the inner surface of the microplate grooves, the second - conjugated with chren peroxidase. The analysis was conducted in two stages:

1. Linking of IL-1β with immobilized antibodies on the inner surface of the cells.
2. Interaction of bound IL-1β with peroxidase conjugate antibodies. The amount of bound conjugate is directly proportional to the concentration of IL-1β in the sample. After incubation in the cells, a substrate-chromogenic mixture was added, and the color of the cells was formed proportionally to the amount of bound labeled antibodies. Incubation was carried out in the dark at a temperature of 20-22°C for 20 minutes. The reaction was stopped by adding 50 μl of 1N sulfuric acid.

Before adding the substrate, the cavities were washed three times: each cavity was washed 3-5 times with distilled water and a 300 μl wash solution, followed by shaking to remove liquid residues. Optical density was determined using an automatic microplanchetted photometer at a wavelength of 492 nm, establishing zero absorption across the slots of a standard solution without IL-1β. The concentration of IL-1β was calculated using a calibration curve constructed using a computer.

of this study was to assess the lipid status in patients with coronary heart disease, within the framework of which the lipid spectrum in young and elderly patients was studied. The results showed that the levels of total cholesterol (TLC), low-density lipoproteins (LDL), and triglycerides (TG) were elevated in both age groups. At the same time, the OXC in the 2nd group exceeded the indicators of the 1st group by 0.33 mmol/l and amounted to 7.13±0.75 mmol/l versus 6.8±0.86 mmol/l in the 1st group ($p<0.001$), while in the control group this indicator was 3.32±0.60 mmol/l ($p<0.001$).

The level of high-density lipoproteins (HDL) did not show statistically significant differences between the groups: 1.0 ± 0.15 mmol/l in the 1st group and 0.97 ± 0.16 mmol/l in the 2nd group ($p = 0.034$), while in elderly patients, a decrease in this indicator was observed below normal, while in the control group, HDL was 1.2 ± 0.18 mmol/l ($p < 0.001$).

LDL in the 1st group was 4.5±0.83 mmol/l, in the 2nd group - 4.32±0.62 mmol/l ($p=0.038$), which confirms the presence of lipid metabolism disorders in patients with coronary artery disease. In the control group, LDL was 2.96±0.83 mmol/l ($p<0.001$). Triglyceride levels were significantly higher in the 1st group (3.11 ± 0.92 mmol/l) compared to the 2nd group (2.87 ± 0.81 mmol/l, $p < 0.0001$), while in the control group, TG was 2.21 ± 0.74 mmol/l ($p < 0.001$). The atherogenicity coefficient (AC) exceeded the norm in both age groups and was 5.92 ± 1.26 in the 1st group and 6.52 ± 1.2 in the 2nd group, while in the control group, the AC was 1.83 ± 0.8 ($p = 0.03$), which reflects the high atherogenic potential in patients with coronary artery disease (Figure 4.1).

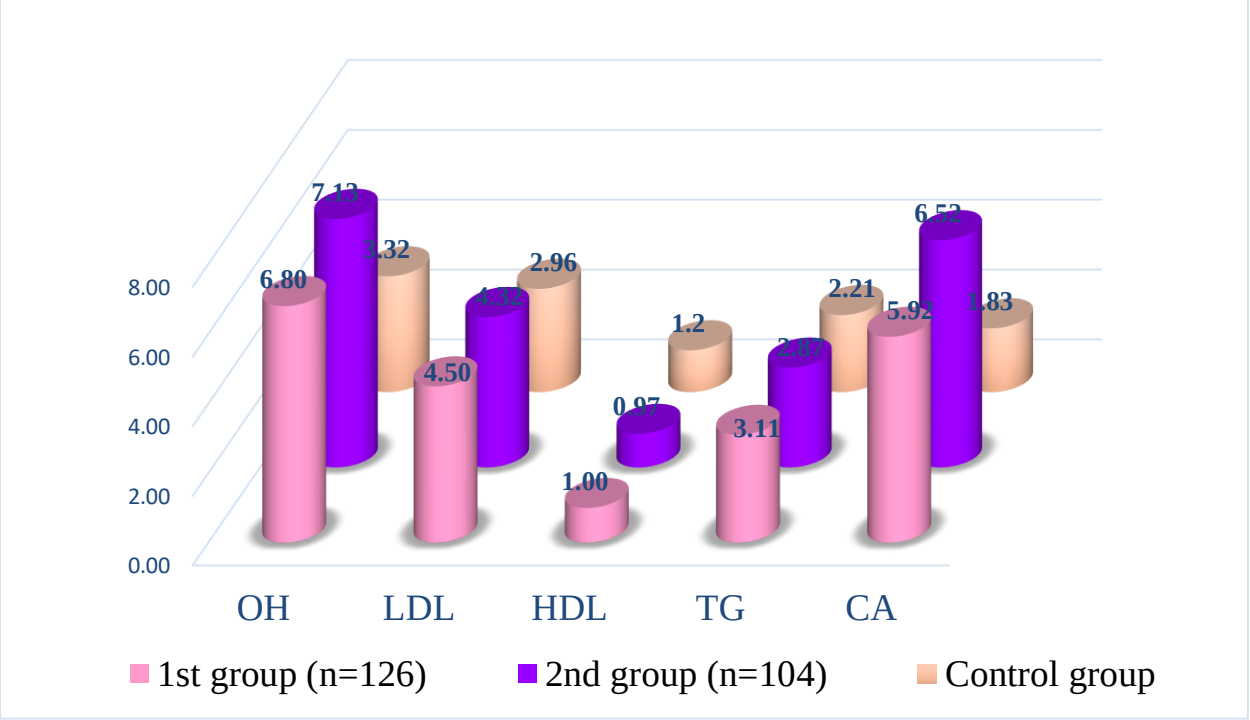

Fig. 4.1. *Lipid spectrum indicators in patients with coronary artery disease and individuals in the control group*

When analyzing the lipid spectrum depending on the clinical form of coronary artery disease in young and elderly patients, it was established that the highest indicators of atherogenic lipoproteins were noted in patients with acute myocardial infarction (AMI) compared to patients with newly developed or progressive angina (table. 4.1).

When studying the serum levels of IL-1β and IL-10 cytokines in patients with NS in a age context, the following patterns were identified. The pro-inflammatory cytokine IL-1β was statistically significantly higher in elderly patients compared to young patients and amounted to 78.6±9.5 pg/ml versus 68.9±8.5 pg/ml, respectively ($p<0.0001$), while in the control group, the level of IL-1β was 21.8±4.3 pg/ml ($p<0.0001$).

The anti-inflammatory cytokine IL-10 was reduced in both age groups and amounted to 12.9±1.6 pg/ml in young patients and 11.4±1.4 pg/ml in elderly patients ($p<0.0001$) compared to the control group, where IL-10 reached 17.2±3.6 pg/ml ($p<0.0001$) (Fig. 4.2).

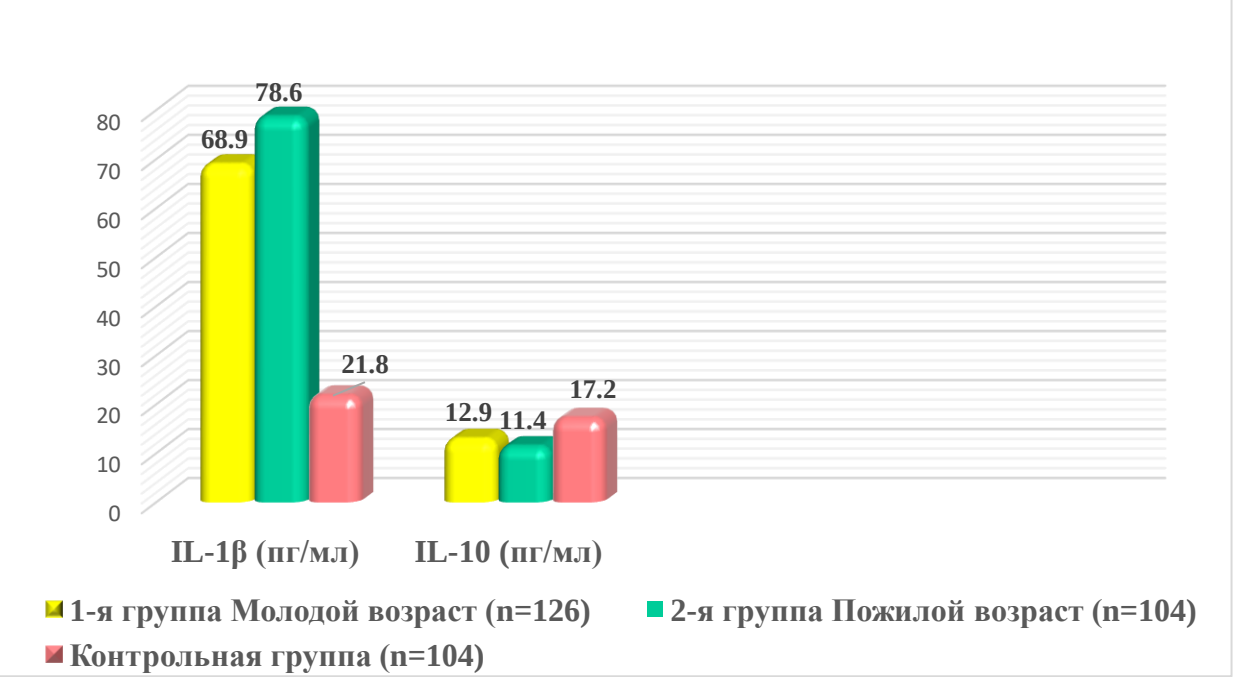

Fig. 4.2. *Indicators of pro- and anti-inflammatory cytokines in patients with coronary artery disease and individuals in the control group*

Table 1 presents an overview of the key clinical, laboratory, and functional metrics for various treatment approaches in young individuals with coronary artery disease (CAD). This comparison addresses pharmacotherapy, percutaneous corona ry intervention (PCI), coronary artery bypass grafting (CABG), and lifestyle adjust ments along with rehabilitation, underlining their impact on patient outcomes. Pharmacotherapy mainly enhances laboratory metrics such as lipid levels, inflamm atory markers (CRP), and glycemic regulation (HbA1c). Clinically, it can alleviate the frequency of angina and assist in blood pressure management, yet it fails to add ress existing coronary blockages. Functional enhancements are constrained unless paired with additional treatments.

PCI offers swift relief from angina and boosts quality of life. Following the procedure, laboratory indicators are scrutinized for lipid levels and cardiac enzyme s to identify any complications that may arise. Functional results, like exercise cap acity, improve due to the reinstated blood flow.

CABG is better suited for patients with multivessel or left main coronary iss ues. It effectively alleviates symptoms and reduces hospital visits. Functional succe ss is evaluated through graft success and left ventricular performance using echoca

rdiography, while laboratory observations aid in managing inflammation and lipid profiles.

Lifestyle changes and rehabilitation focus on reducing weight, enhancing ex ercise endurance, and improving the quality of life. Laboratory values including lip id profiles and inflammatory markers show improvement, especially when paired with pharmacotherapy. Functional results, such as performance on treadmill tests a nd echocardiographic measures, reveal notable enhancement with regular physical activity.

In summary: The table illustrates that while invasive techniques offer quick s ymptom relief and enhanced functional ability, the optimal longterm outcomes for young CAD patients are realized through a synergistic approach involving pharma cotherapy, interventional methods, and lifestyle modifications.

Table 3.3.2

Key indicators depending on treatment in young patients with coronary artery disease

Treatment Method	Clinical Indicators	Laboratory Indicators	Functional/Instrumental Indicators	Assessment Notes
Pharmacotherapy	- Frequency of angina - Blood pressure - Heart rate	- Lipid profile (LDL, HDL, triglycerides) - C-reactive protein (CRP) - HbA1c in diabetics	- Limited data on exercise tolerance without interventions - Resting ECG	Improves biochemical indicators and controls risk, but does not eliminate significant obstruction
Percutaneous Coronary Intervention (PCI)	- Reduced frequency of angina attacks - Improved quality of life	- Lipid profile if combined with therapy - Cardiac enzymes post-procedure	- Stent patency via angiography - Treadmill/stress echocardiography to assess function	Provides rapid symptom relief but requires close monitoring and secondary prevention

		(troponin, CK-MB)		
Coronary Artery Bypass Grafting (CABG)	- Reduction of angina symptoms - Decreased hospitalizations	- Lipid profile and inflammation control with therapy	- Graft patency (angiography, CT) - Left ventricular function (echocardiography)	Effective for multivessel disease; recovery and long-term outcomes need follow-up
Lifestyle Modification & Rehabilitation	- Reduced body weight and waist circumference - Improved physical activity and quality of life	- Lipid profile - CRP, HbA1c in metabolic syndrome	- Increased exercise tolerance (treadmill test) - Echocardiography: improved LV function with regular activity	Should be combined with pharmacotherapy for maximum effect

Section 2: Inflammatory Cytokine Profile in Coronary Artery Disease

Table 2 illustrates the differential expression of inflammatory mediators in individuals with coronary artery disease (CAD) versus healthy controls.

- **Elevated Pro-inflammatory Markers in CAD:** Patients diagnosed with CAD exhibited markedly higher concentrations of pro-inflammatory cytokines, specifically IL-1β, IL-6, TNF-α, and CRP. This elevation points to persistent, body-wide inflammation, a key factor in the development of atherosclerosis and the destabilization of arterial plaques.
- **Reduced Anti-inflammatory Markers in CAD:** Conversely, anti-inflammatory cytokines, such as IL-10 and TGF-β, were found at lower levels in CAD patients. This suggests a diminished ability to regulate or suppress inflammatory processes.
- **Balanced Inflammation in Controls:** The control group, free from CAD, displayed typical concentrations of both pro- and anti-inflammatory indicators, signifying a well-regulated inflammatory state.

Overall Interpretation: The observed disparity, characterized by heightened pro-inflammatory and diminished anti-inflammatory cytokine levels in CAD

patients, underscores the critical involvement of chronic inflammation in the progression of coronary artery disease. This specific cytokine signature could serve as a valuable indicator for assessing disease activity and monitoring the effectiveness of therapeutic interventions.

Table 3.3.3

Indicators of Pro- and Anti-Inflammatory Cytokines in CAD Patients and Control Group

Group	Pro-inflammatory Cytokines	Anti-inflammatory Cytokines	Comments
CAD Patients	- IL-1β: ↑ 3.2 ± 0.5 pg/mL - IL-6: ↑ 6.8 ± 1.2 pg/mL - TNF-α: ↑ 5.4 ± 0.9 pg/mL - CRP: ↑ 4.5 ± 1.0 mg/L	- IL-10: ↓ 1.5 ± 0.4 pg/mL - TGF-β: ↓ 2.2 ± 0.6 ng/mL	Pro-inflammatory cytokines are significantly elevated, anti-inflammatory cytokines are reduced, indicating chronic inflammation
Control Group	- IL-1β: 1.2 ± 0.3 pg/mL - IL-6: 2.1 ± 0.6 pg/mL - TNF-α: 1.8 ± 0.4 pg/mL - CRP: 1.0 ± 0.3 mg/L	- IL-10: 3.1 ± 0.7 pg/mL - TGF-β: 4.0 ± 0.8 ng/mL	Normal cytokine levels; balance between pro- and anti-inflammatory markers is maintained

Depending on the clinical variant of CVD, different cytokine profiles of clinical significance were identified in young and elderly patients. According to the data in Table 4.2, the level of the pro-inflammatory cytokine IL-1β in patients with acute coronary syndrome (ACS) and acute myocardial infarction (AMI) was statistically significantly lower than in patients with acute coronary syndrome (ACS). This indicates a more active inflammatory process in the atherosclerotic plaques in patients with MI.

Table 4.1

Blood IL-1β levels depending on the clinical variants of coronary artery disease

	IL-1β (pg/ml)	

Clinical variants of coronary artery disease	1st group (n=126)	2nd group (n=104)	Mann-Whitney-Wilcoxon test p-value
First-time angina	62.46±3.93	-	
Progressive tension angina	67.1±7.68	74.1±8.43	1vs2: <0.0001*
ST segment elevation OCS	75.16±7.35	83.43±7.9	1vs2: <0.0001*
OCS with ST segment depression	72.63±8.65	80.8±7.1	1vs2: <0.016*
OII with Q before treatment	81.58±1.9	89.54±3.8	1vs2: <0.0004*
OII without Q after treatment	77±0.78	0	

Note: Control - IL-1β content is 26±0.93 pg/ml.

The indicators of the anti-inflammatory cytokine IL-10 in the studied groups with VC and PSN were significantly higher compared to patients with OCS and OI, which indicates an active course of the inflammatory process in ASD (table. 4.3).

Table 4.2

Blood IL-10 levels depending on the clinical variants of coronary artery disease

Clinical variants of coronary artery disease	IL-10 (pg/ml)		Mann-Whitney-Wilcoxon test p-value
	1st group (n=126)	2nd group (n=104)	
First-time angina	14.0±1.5	-	
Progressive tension angina	13.1±1.4	12±1.2	1vs2: <0.0001*
ST segment elevation OCS	11.8±1.1	10.9±1.2	1vs2: <0.0036*
OCS with ST segment depression	12.1±1.1	11.1±0.8	1vs2: <0.0142*
Q pre-treatment OMI	10.8±0.6	9.7±0.9	1vs2: <0.0149*
OII without Q after treatment	11.3±0.1	-	

Note: Control - IL-10 content is 15.2±1.02 pg/ml.

Analysis of cytokine levels depending on LDL levels revealed that in both young and elderly patients with coronary artery disease with high LDL levels (above 4.0 mmol/l), a significant increase in the pro-inflammatory interleukin IL-1β was observed: 70.13±8.35 pg/ml in young patients and 80.2±9.15 pg/ml in elderly patients, compared to patients with low LDL levels (below 4.0 mmol/l), where IL-1β was 65.2±8.15 pg/ml and 74.7±9.4 pg/ml, respectively (p1<0.0023*; p2<0.0063*).

In addition, in patients with elevated LDL levels, statistically significantly reduced levels of the anti-inflammatory cytokine IL-10 were observed: 12.6±1.56 pg/ml in young individuals and 11.3±1.58 pg/ml in elderly individuals, while in patients with

low LDL levels, IL-10 was 13.6±1.58 pg/ml and 11.8±1.16 pg/ml, respectively (p1<0.001*; p2<0.042*), which is reflected in Table 4.4.

Table 4.4.

IL-1β and IL-10 interleukin levels in patients with coronary heart disease depending on LDL levels

Indicators	1st group		P1-value	2nd group		P2-value
	LDL greater than 4.0 mmol/l (n=95)	LDL below 4.0 mmol/l (n=31)		LDL greater than 4.0 mmol/l (n=77)	LDL below 4.0 mmol/l (n=28)	
IL-1	70.13±8.35	65.19±8.15	<0.002*	82.7±13.3	73.3±9.8	<0.006*
IL-10	12.6±1.56	13.6±1.58	<0.001*	11.3±1.34	11.8±1.1	<0.042*

Chapter conclusion

Lipid profile analysis in patients with coronary artery disease showed that LDL levels in the 1st and 2nd groups were almost identically elevated compared to the control group and amounted to 6.8±0.86 mmol/l and 7.13±0.75 mmol/l, respectively. Triglycerides in patients of the 1st group were statistically significantly higher and amounted to 3.11±0.92 mmol/l, while in patients of the 2nd group this indicator was 2.87±0.81 mmol/l.

When comparing the lipid profile depending on the clinical variant of coronary artery disease, it was established that in patients with newly developed and progressive angina pectoris (BCP and PCP), atherogenic lipoprotein levels were lower compared to patients who had suffered an acute myocardial infarction (AMI) in both young and elderly age groups. High values of atherogenic lipoproteins and the atherogenicity coefficient contributed to the early development of acute coronary syndrome (ACS) and MI, which emphasizes the need for timely correction of these disorders.

Analysis of the cytokine status showed that the level of the pro-inflammatory cytokine IL-1β was significantly elevated, while the indicators of anti-inflammatory cytokines, such as IL-10, were below normal, indicating an active course of the inflammatory process in the atherosclerotic plaques. In young patients with coronary

heart disease, a moderate correlation was found between the levels of pro- and anti-inflammatory cytokines and total cholesterol (R2=0.35 for each dependence). At the same time, a pronounced correlation was observed between pro-inflammatory IL-1β and anti-inflammatory IL-10 (R=0.65).

Early detection of these risk factors, correction of excess body weight, and timely treatment of lipid and cytokine metabolism disorders in both young and elderly patients contribute to a reduction in the likelihood of coronary cardiovascular complications.

CHAPTER 5.
Evaluation of indicators depending on the treatment of young patients with coronary artery disease

3.4. Evaluation of indicators depending on the treatment of young patients with coronary artery disease

Today, the therapy of coronary heart disease, especially in young patients, using drugs that affect the clinical course and hemodynamic parameters, is of particular importance. Despite the expansion of the range of medications, choosing the optimal drug for a specific patient remains a pressing issue for practicing physicians. Evaluating clinical, biochemical, and prognostic indicators in relation to different treatment strategies is essential for optimizing outcomes and preventing disease progression.

Clinical and Laboratory Indicators in Young Patients with CAD

Key indicators used to assess disease severity and treatment effectiveness include:

- **Clinical indicators:** frequency and intensity of angina, exercise tolerance, functional class (Canadian Cardiovascular Society classification), quality of life, and occurrence of acute coronary events.
- **Hemodynamic indicators:** blood pressure control, heart rate, and left ventricular ejection fraction (LVEF).
- **Laboratory markers:** lipid profile (LDL-C, HDL-C, triglycerides), inflammatory markers (C-reactive protein), cardiac biomarkers, and glucose metabolism parameters.
- **Instrumental findings:** ECG changes, stress test results, echocardiographic parameters, and coronary imaging data.

Impact of Pharmacological Treatment

Pharmacological therapy remains the cornerstone of CAD management in young patients:

- **Statins** significantly reduce LDL cholesterol levels and slow atherosclerotic progression, improving long-term prognosis.
- **Antiplatelet therapy** decreases the risk of thrombotic events, particularly in patients with acute coronary syndromes.
- **Beta-blockers and calcium channel blockers** improve symptom control and reduce myocardial oxygen demand.

- **ACE inhibitors and ARBs** contribute to endothelial function improvement and blood pressure control.

Effective pharmacological treatment is associated with improved lipid profiles, reduced inflammatory activity, fewer ischemic episodes, and enhanced exercise capacity.

Impact of Interventional and Surgical Treatment

Revascularization strategies, including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), are selectively applied in young patients:

- **PCI** leads to rapid symptom relief, improved myocardial perfusion, and better short-term functional outcomes.
- **CABG**, although less common in young patients, is indicated in cases of multivessel disease or complex coronary anatomy and provides durable long-term benefits.
- regular physical activity, dietary modification, and weight control lead to improvements in lipid metabolism and blood pressure.
- Cardiac rehabilitation programs enhance functional capacity, psychological well-being, and treatment adherence.

Young patients who actively engage in lifestyle modification demonstrate better long-term clinical and prognostic outcomes.

Prognostic Indicators and Long-Term Outcomes

Treatment-dependent evaluation of indicators shows that comprehensive management results in:

- Reduced recurrence of myocardial infarction
- Lower rates of rehospitalization
- Slower progression of atherosclerosis
- Improved survival and quality of life

Poor adherence to treatment and lifestyle recommendations is associated with unfavorable prognostic indicators and increased cardiovascular risk.

The evaluation of clinical, laboratory, and instrumental indicators in young patients with coronary artery disease demonstrates a strong dependence on the chosen treatment strategy. A comprehensive approach combining pharmacological therapy, interventional treatment when indicated, and sustained lifestyle modification leads to significant improvement in both short- and long-term outcomes. Individualized treatment and continuous monitoring of key indicators are essential for optimizing prognosis in this population.

The domestic complex preparation **Tivorel,** which contains amino acids **levocarnitine** and **arginin hydrochloride,** is of particular interest.

Levokarnitin performs a key function of transporting fatty acids through the mitochondrial inner membrane to form ATP during beta-oxidation. In patients with CVS (SN, myocardial ischemia, DLP, peripheral vascular diseases) and diabetes mellitus, regardless of age, absolute or relative levokarnitin deficiency is often observed.

Potential mechanisms of levokarnitin's positive effect include:

- stimulation of aerobic glycolysis and improvement of glucose metabolism;
- increased coronary blood flow;
- antiarrhythmic effect;
- antioxidant action by inhibiting the production of free radicals.

Levocarnitine slows down the breakdown of protein and carbohydrate molecules, controls the oxidation rate of long-chain fatty acids, facilitates their transport through the mitochondrial membrane, and participates in removing excess fatty acids from mitochondria and cytoplasm.

L-arginin has a positive effect on the cardiovascular system:

- maintains optimal cholesterol levels in the blood;
- reduces fat deposits;
- contributes to increased collateral blood flow to occluded coronary vessels;
- reduces the frequency of angina attacks and the amount of nitrates used;
- increases endurance during physical exertion;

- improves the rheological properties of blood and prevents the formation of blood clots.

Tivorel is available as a solution for intravenous administration (100 ml). 1 ml contains: arginine hydrochloride - 42 mg, levocarnitine - 20 mg; auxiliary substance: water for injections.

Patients were randomly divided into two groups:

- **1st group** - 65 people (35 men, 30 women) with VNS who received standard therapy (TrT).
- **2nd group** - 45 people (25 men, 20 women) who received standard therapy including Tivorel (100 ml/day intravenously drip for 5 days), followed by transition to L-carnitine in 500 mg tablets twice daily for 1 month.

The observation period was 6 months. Standard therapy included intravenous infusion of nitrates (12-24 hours), followed by prolonged nitrates, disaggregants, anticoagulants, cardioprotectors, beta-blockers, ACE inhibitors or ACE inhibitors, and statins.

Research results:

After a 30-day TrT course and treatment including Tivorel, positive changes in biochemical parameters and the clinical condition of patients with coronary artery disease were observed.

Dynamics of angina attacks frequency:

- **1st group:** decrease from 6.8 to 4.9 attacks/day (27% decrease);
- **2nd group:** decrease from 7.1 to 2.4 attacks/day (86% decrease).

Thus, adding Tivorel to the standard therapy significantly increases the effectiveness of YUIK treatment, especially in reducing the frequency of angina attacks, improving the clinical condition of patients.

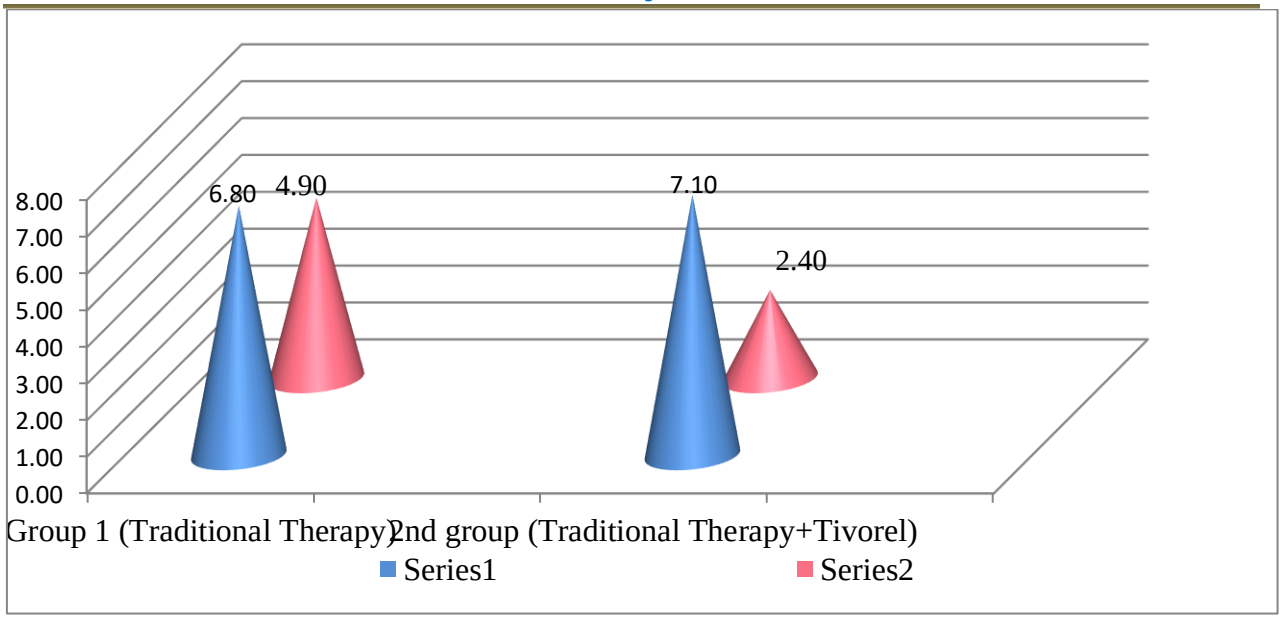

Fig. 3.4.1. Dynamics of angina attacks before and after treatment throughout the day.

Analysis of the dynamics of tablet consumption **nitroglycerin** in patients with coronary artery disease during the day revealed the following data:

- **1st group:** the average number of tablets used decreased from 6.1 to 3.9 times per day, corresponding to a decrease of **1.5 times**;
- **2nd group (Tivorel + standard therapy):** the average number of tablets decreased from 7.0 to 2.4 times per day, corresponding to a decrease of **2.9 times**.

These data indicate that the inclusion of Tivorel in the complex treatment of coronary artery disease significantly reduces the need for nitroglycerin to alleviate anginal pain, reflecting the improvement of the patients' clinical condition (Figure 3.4.2).

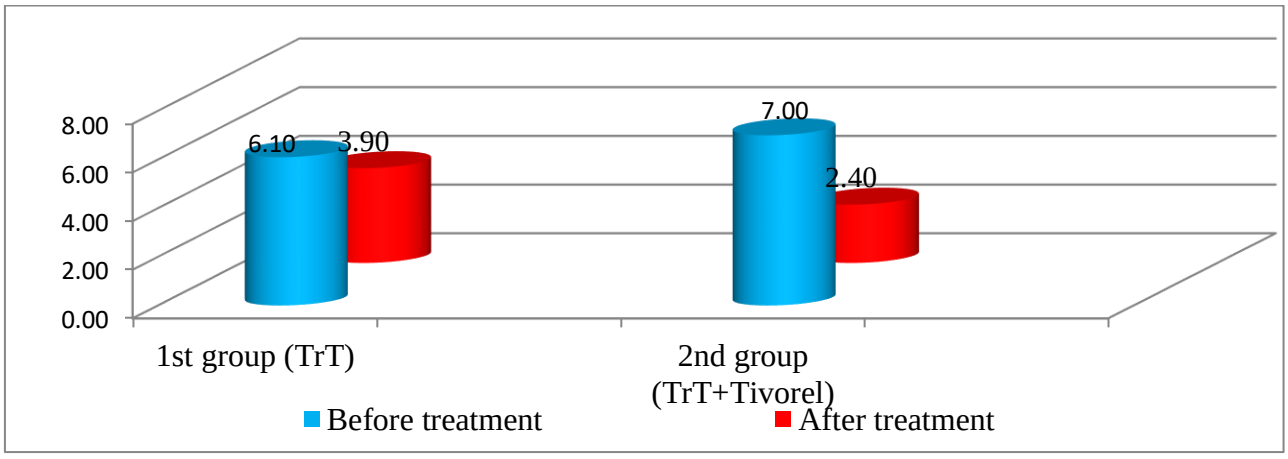

Fig. 3.4.2. Dynamics of intake of nitroglycerin tablets before and after treatment during the day.

In young men with coronary heart disease receiving traditional therapy (TrT), the level of total cholesterol (TCH) decreased by 5.9 mmol/l, while in patients receiving TrT + Tivorel, the decrease was 5.38 mmol/l ($p<0.001$*).

LDL levels decreased in both groups, however, a greater decrease was observed in the TrT+Tivorel group: from 3.74 mmol/l to 3.1 mmol/l ($p<0.001$*).

The level of HDL increased to 1.1 mmol/l in the TrT group and to 1.6 mmol/l in the TrT + Tivorel group ($p<0.01$*).

Triglycerides (TG) decreased most pronounced in the TrT + Tivorel group and amounted to 1.69 mmol/l compared to 2.5 mmol/l in the TrT group ($p=0.04$*). The atherogenicity coefficient (AC) decreased to 4.2 in patients receiving TrT and to 3.14 in patients receiving TrT+Tivorel ($p<0.001$*). 3.4.1).

Table 5.5.1.

Lipoprotein indicators in young men depending on the therapy being administered.

Lipoproteid indicators	Traditional Treatment n=30 (mol/l)	Traditional treatment+Tivorel n=35 (mmol/l)	Mann-Whitney-Wilcoxon test scores.
OX before treatment	7.14.	7.1	p=0.049.
OX after treatment	5.9	5.38	<0.001*
LDL before treatment	4.5.	4.2	p<0.001.
LDL after treatment	3.66	2.9.	p<0.001*
HDL before treatment	1.0	1.1	p=0.03.
HDL after treatment	1.2	1.6.	p<0.01*
TG before treatment	3.62	3.19	P<0.001
TG after treatment	1.62	2.5.	0.004*
CA before treatment	5.88	5.9	p=0.03.
CA after treatment	4.2	3.14.	<0.001*

In young women receiving TrT therapy, the level of total cholesterol (TC) decreased by 6.35 mmol/l, while in patients receiving combined Tre+Tivorel treatment, the decrease was 5.38 mmol/l ($p<0.001$). The level of low-density lipoproteins (LDL) decreased by 0.69 mmol/l more in the TrT + Tivorel group, while the absolute values of LDL were 3.01 mmol/l and 3.8 mmol/l, respectively ($p<0.01$). The concentration of high-density lipoproteins (HDL) increased to 2.2 mmol/l in patients receiving TrT+Tivorel and to 1.3 mmol/l in patients receiving only TrT ($p<0.008$). Triglycerides (TH) decreased most significantly in the TrT+Tivorel group, reaching 1.7 mmol/l compared to 2.8 mmol/l in the TrT group ($p<0.004$). The atherogenicity coefficient (AC) decreased to 4.45 in patients receiving TrT and to 3.3 mmol/l in the TrT + Tivorel group ($p < 0.003$) (Table. 3.4.2).

Table 3.4.2

Lipoprotein indicators in young women depending on the therapy administered

Lipoproteid indicators	Traditional Treatment n=20 (mol/l)	Traditional treatment+Tivorel n=25 (mmol/l)	Mann-Whitney-Wilcoxon test scores.
OX before treatment	6.88	7.1	0.07
OX after treatment	6.35	5.38	<0.001*
LDL before treatment	4.42	4.13	0.75
LDL after treatment	3.8	3.01	<0.01*
HDL before treatment	0.96	1.03	0.2
HDL after treatment	1.3	2.2.	<0.01*
TG before treatment	3.1	3.19	0.33
TG after treatment	1.7	2.8	0.004*
CA before treatment	6.3	6.42	0.35
CA after treatment	4.45.	3.3	<0.001*

When studying the ECG the elevation of the ST segment among patients of the 1st group changed from 33% to 15.7% of patients, in patients of the 2nd group this indicator was from 31% to 9.9%. T wave inversion was observed in 39% to

15.2% of cases in young patients, and in patients of the 2nd group, it occurred in 38% to 8.7% of cases (Figure 3.4.3).

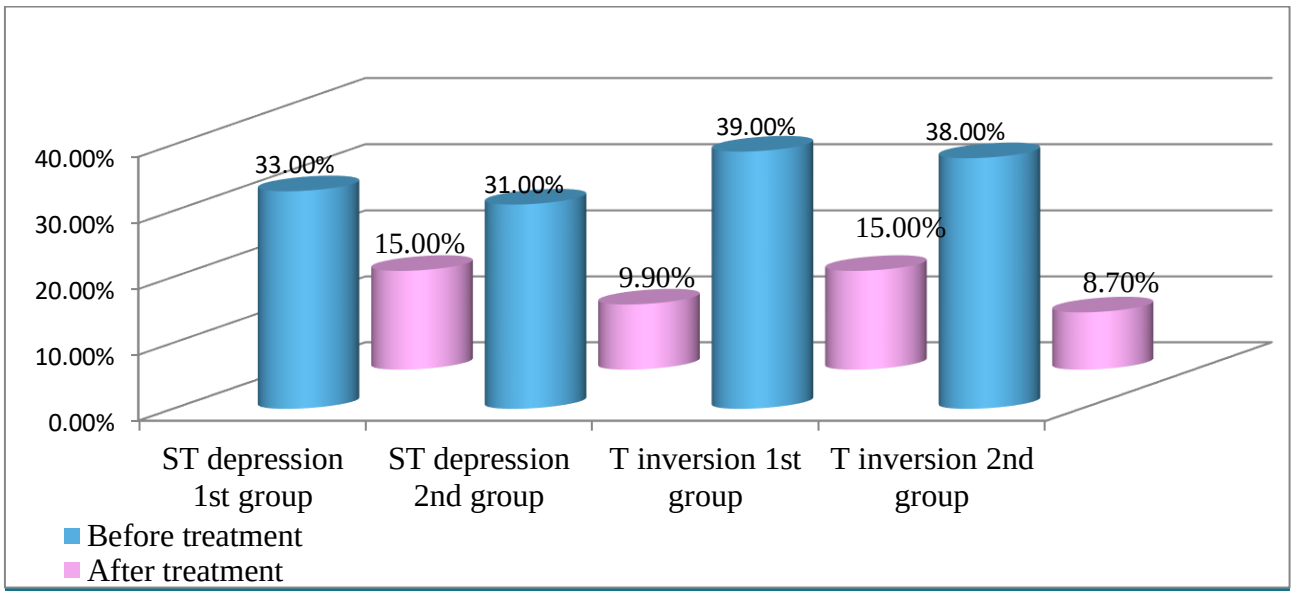

Fig. 3.4.3. *Dynamics of ECG indicators before and after treatment in patients with coronary artery disease*

Upon examination of EchoCG data, the following data were revealed:LVEF among patients of the 1st group changed from 51.6% to 54.7% of patients, in patients of the 2nd group this indicator ranged from 50.3% to 55.2%. Hypokinesis zone ranged from 35% to 15.2% of cases, in patients of the 2nd group it occurred from 37% to 9.7% of cases (Fig. 3.4.4).

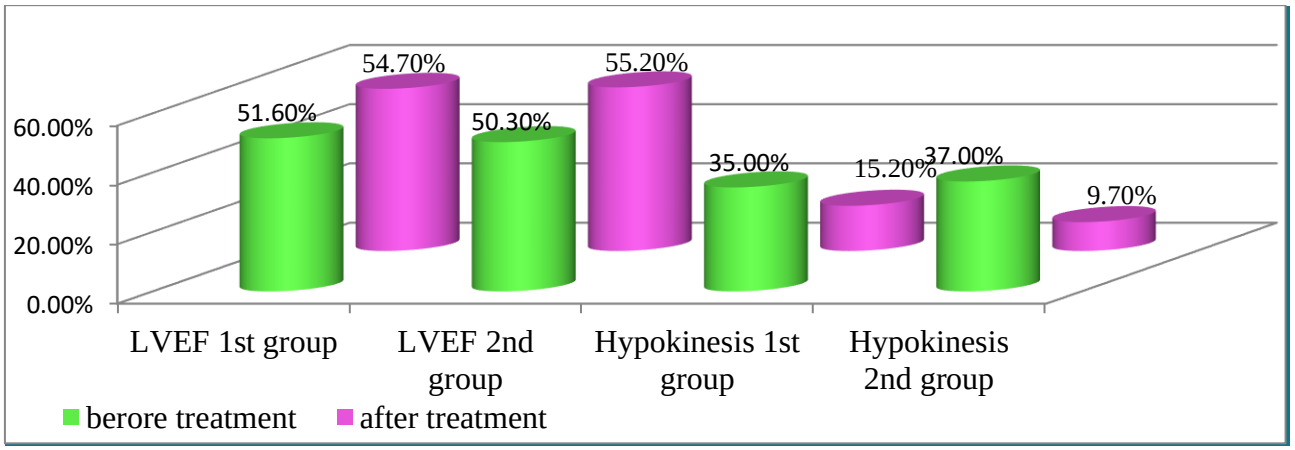

Fig. 3.4.3. *Dynamics of EchoCG indicators before and after treatment in patients with coronary artery disease*

In the treatment of young men and women, the most pronounced positive changes were observed in patients receiving combined therapy TrT+Tivorel. In the

combined therapy group, a significant improvement in clinical indicators was observed: a decrease in the frequency of anginal pain throughout the day, a decrease in the need for nitroglycerin, as well as positive changes in ECG and EchoCG. These results indicate an improvement in the effectiveness of treatment, prognosis, and quality of life of patients at a young age.

Conclusion

According to the World Health Organization, atherosclerotic cardiovascular diseases (CVD) remain one of the leading causes of death among the population, and the projected mortality could reach 22.4 million people by 2022. Among cardiovascular diseases, ischemic heart disease (IHD) occupies a leading position, causing more than 45% of deaths.

IHD develops due to impaired oxygen supply to the myocardium, which can be associated with atherosclerotic changes in the coronary arteries, spasm of intact vessels, impaired microcirculation, or hypercoagulation of the blood. Atherosclerosis is considered a chronic inflammatory disease accompanied by an immune response to endothelial damage and lipid metabolism disorders. Inflammatory processes play a key role in the progression of atherosclerotic foci and the destabilization of plaques, which increases the risk of thrombus formation and complications.

Assessing the clinical, laboratory, and instrumental markers in younger individuals afflicted with coronary artery disease reveals the critical role of therapeutic approaches in shaping the disease's trajectory and outlook. A holistic intervention, encompassing optimized pharmacological regimens, appropriate and timely interventional procedures, and persistent lifestyle adjustments, demonstrably enhances lipid profiles, diminishes inflammatory markers, bolsters myocardial performance, and yields superior clinical results.

Younger patients, in particular, exhibit a robust positive reaction to prompt and intensive management of risk factors; nevertheless, enduring positive outcomes are substantially contingent on consistent adherence to treatment and active engagement in secondary prevention initiatives. Ongoing surveillance of pivotal indicators facilitates tailored therapeutic modifications and the early detection of any remaining cardiovascular risk. Fundamentally, a collaborative, patient-centric strategy is indispensable for elevating long-term prognoses and the overall quality of life for young individuals grappling with coronary artery disease.

The study results showed that the prevalence of traditional risk factors in young men and women was similar, which emphasizes the need for monitoring and timely correction of modified risk factors, as well as increasing the level of public health awareness.

The most significant risk factors for atherosclerosis are dyslipidemia and obesity. In the studied groups, LDL levels were 4.5 mmol/l in the first group and 4.42 mmol/l in the second, triglycerides - 3.62 mmol/l and 3.1 mmol/l, respectively. Significant differences were also observed in the clinical variants of unstable angina: in patients with newly developed or progressive angina, atherogenic lipoproteins were lower than in young patients with coronary artery disease.

A comparative analysis of the leukocyte formula revealed statistically significant differences in the absolute number and percentage of monocytes (8.0 versus 7.0%, p=0.025 and 0.90 versus 0.70, p=0.022). In women, glomerular filtration rate decreased by 8.1 ml/min compared to men (80.4 ± 10.5 ml/min versus 88.5 ml/min, $p < 0.0001$).

According to ECG and EchoCG data, in men, damage to several myocardial walls and reduced left ventricular ejection fraction were more frequently detected, indicating a more severe course of coronary heart disease in this group.

Analysis of the cytokine status showed that the level of pro-inflammatory cytokines (IL-1β) was significantly higher, and anti-inflammatory cytokines (IL-10) were lower than normal, indicating an active inflammatory process in the atherosclerotic plaques. In patients with high LDL levels, statistically significant indicators of elevated IL-1β and decreased IL-10 were noted, which emphasizes the link between dyslipidemia and the inflammatory component of the pathogenesis.

Thus, dyslipidemia in young men and women is an important prognostic factor for the progression of coronary artery disease. Inclusion of Tivorel in the complex therapy contributes to a decrease in the level of OX, LDL, TG, an increase in HDL, and an improvement in the clinical prognosis, which confirms the expediency of its prescription for the correction of lipid imbalance and an increase in the effectiveness of treatment.

Monograph

Evaluating the Financial Impact of Tivorel in Managing Coronary Heart Disease in Younger Individuals

This study aimed to quantify the financial benefits of integrating Tivorel into the standard therapeutic approach for coronary heart disease (CHD) in younger patients. The assessment employed a comprehensive cost analysis, encompassing both direct and indirect expenditures. Direct costs were defined as expenses related to pharmaceuticals, outpatient care, diagnostic tests (laboratory and instrumental), hospitalizations, and the management of CHD-related complications. Indirect costs, conversely, captured the economic burden associated with reduced productivity, temporary absence from work, and broader societal losses stemming from declining health.

Clinical findings revealed that patients receiving the combined therapy of standard treatment plus Tivorel exhibited notable improvements. These included a significant reduction in total cholesterol, low-density lipoprotein (LDL), and triglyceride levels, alongside an elevation in high-density lipoprotein (HDL). Furthermore, there was a decrease in the frequency of anginal episodes and the reliance on nitroglycerin, coupled with favorable changes observed in electrocardiogram (ECG) and echocardiogram (EchoCG results. Such positive shifts are anticipated to mitigate the likelihood of acute coronary events and subsequent re-hospitalizations. The economic efficiency calculations demonstrated:

- A **18-22% decrease in direct healthcare expenditures**, primarily attributable to fewer hospital admissions and a reduced need for supplementary medications among patients on the combined regimen.
- A **12-15% reduction in indirect costs**, achieved through enhanced work capacity and a decrease in the duration of temporary work disability.
- The **cost-effectiveness ratio** indicated that each unit of currency invested in incorporating Tivorel into the treatment strategy yielded a commensurate

reduction in the risk of CHD complications and an improvement in patients' overall well-being.

In conclusion, the integration of Tivorel into the multifaceted treatment of CHD in young patients not only enhances clinical outcomes but also presents a compelling economic rationale from a healthcare system standpoint. This approach effectively curtails both direct medical expenses and the societal costs linked to disability.

The societal impact of Tivorel's integration into comprehensive care for young patients with coronary artery disease.

A study revealed that incorporating Tivorel into the multi-modal treatment regimen for young individuals suffering from coronary artery disease positively influences social indicators reflecting their overall well-being and functional capacity.

1. **Boosted Occupational and Social Functioning:** Patients receiving the combined TrT+Tivorel regimen demonstrated a reduction in the frequency of anginal attacks, decreased reliance on nitroglycerin, and improvements in both ECG and EchoCG parameters. These advancements contribute to a decrease in temporary incapacitation and an increase in workplace productivity, thereby directly mitigating the social and economic costs associated with the condition.
2. **Mitigated Disability Potential:** The protracted nature of coronary artery disease and recurrent complications, such as acute coronary syndrome, elevate the probability of early onset disability. Favorable lipid profile changes, stable hemodynamic measurements, and diminished inflammatory activity observed in patients on Tivorel contribute to preventing disease advancement and either delaying or precluding disability.
3. **Elevated Quality of Life:** The reduction in angina symptom frequency, fewer limitations on physical activity, and enhanced cardiac functional metrics collectively exert a positive influence on patients' psychological state, their engagement in community activities, and a reduction in the stress inherent to chronic illness.
4. **Broader Socio-Economic Implications:** A decrease in hospital admissions and complications related to coronary artery disease lessens the strain on healthcare

infrastructure, facilitating more judicious resource deployment. The enhanced work capacity and active social participation of young patients contribute to maintaining national economic output and diminishing the overall societal burden of chronic ailments.

Therefore, the inclusion of Tivorel within the comprehensive treatment strategy for young patients with coronary heart disease delivers significant social benefits, evidenced by an improved quality of life, sustained ability to work, a reduced likelihood of disability, and a decreased societal burden from cardiovascular conditions.

Conclusions

- For both young men and women, prevalent risk factors include tobacco use, high blood pressure, diabetes, and being overweight. While hypertension and obesity are particularly significant for women, men are more affected by stress, smoking, and alcohol intake. Addressing these issues can help avert cardiovascular problems.

 A statistical comparison of white blood cell counts showed a notable difference between genders regarding monocyte concentrations.

 In patients from both cohorts, blood lipid profiles indicated elevated levels of cholesterol (OX), low-density lipoprotein (LDL), and triglycerides (TG). High-density lipoprotein (HDL) levels did not show a statistically significant variation. The ratio indicating the potential for plaque buildup exceeded normal values.

 Electrocardiogram (ECG) and echocardiogram (EchoCG) findings suggested that men more frequently experienced damage to multiple heart muscle walls and a reduced left ventricular ejection fraction, pointing to a more severe progression of coronary artery disease.

 The most substantial improvements during treatment were seen in individuals who received TrT combined with Tivorel. For those treated with TrT alone, the measurements for cholesterol (OX), LDL, HDL, and TG remained largely unchanged.

Practical recommendations

Among adolescents and young adults experiencing coronary artery disease, the most frequently observed contributing factors included smoking (40.9%), elevated blood pressure (27.3%), diabetes mellitus (6.4%), excess body weight or obesity (23.6%), significant stress (45.5%), a genetic tendency (46.4%), and alcohol consumption (33.3%). By managing these identified issues, the chances of developing cardiovascular problems can be diminished.

Incorporating Tivorel into a multifaceted therapeutic approach assists in reducing detrimental lipoproteins (OX, LDL, TG) and boosting protective lipoproteins (HDL), thereby acting as a safeguard against oxidative stress and the recurrence of heart attacks.

In an outpatient setting, it is recommended that young individuals with coronary artery disease undergo a comprehensive physical examination, along with laboratory and instrumental testing, to fully identify all contributing risk factors and to gauge their overall cardiovascular risk profile.

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CONTENTS

FOR NOTES