MINISTRY OF HEALTHCARE OF THE REPUBLIC OF UZBEKISTAN

SAMARKAND STATE MEDICAL UNIVERSITY

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DIFFERENTIATED APPROACH TO THE DIAGNOSIS AND TREATMENT OF CORONARY HEART DISEASE DESTABILIZATION IN WORKING-AGE MAN

(monograph)

TASHKENT 2025

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This monograph includes the latest modern data on coronary heart disease, the peculiarity of its course, etiopathogenetic risk factors predisposing to the development or progression of this disease, especially in men of working age. The literary review was compiled on the basis of modern literary sources from the CIS countries and foreign countries. When analyzing the literature, the authors were able to identify several predisposition factors for the development of coronary heart disease in working-age men, including dyslipidemia and cytokine imbalance. Based on our own clinical, laboratory, and immunological studies, we describe the characteristics of the clinical course and treatment strategies for coronary heart disease in working-age men, depending on etiopathogenetic risk factors.

ACCEPTED ABBREVIATIONS

AH	Arterial Hypertension
PW LV	Posterior Wall of the Left Ventricle
LAH	Left Atrial Hypertrophy
LVH	Left Ventricular Hypertrophy
RAH	Right Atrial Hypertrophy
AD	Aortic Diameter
CHD	Coronary Heart Disease
MI	Myocardial Infarction
BMI	Body Mass Index
EDD	End-Diastolic Dimension
ESD	End-Systolic Dimension
PA	Pulmonary Artery
LV	Left Ventricle
HDL-C	High-Density Lipoprotein Cholesterol
LDL-C	Low-Density Lipoprotein Cholesterol
IVS	Interventricular Septum
ACS	Acute Coronary Syndrome
TC	Total Cholesterol
CO	Cardiac Output
DM	Diabetes Mellitus
HF	Heart Failure
CVE	Cardiovascular Event
EF	Ejection Fraction
ECHO	Echocardiogram
ECG	Electrocardiogram
EAH	Electrical Axis of the Heart
EA	Elektrical axis of heart
HR	Heart Rate

FOREWORD

Coronary heart disease (CHD) is the most widespread among cardiovascular diseases (CVD). This condition is characterized by a persistent increase in rates of morbidity, disability, and mortality in both developed and developing countries., making it a particularly concerning issue when it affects working-age individuals. Analysis of mortality cases from IHD by age shows that approximately 30% of these fatalities occur in younger individuals (over 560,000 people annually), with 80% of them being men. This mortality rate is 4.1 times higher compared to women. The mortality rate from IHD in individuals aged 25-44 is 10 per 100,000. The involvement of a young person in cardiovascular disease not only causes personal tragedy but also inflicts considerable social and economic harm on society due to a drastic decline in productivity, as well as expenses related to treatment, rehabilitation, and recovery of the affected individual.

In Western countries, about 30% of the population with chronic coronary heart disease die from various coronary artery (CA) damage, and the increase in these figures among working-age individuals directly impacts the future of the country and society as a whole. In men aged 20 to 44, the incidence of ischemic heart disease (IHD) ranges from 5% to 8%, whereas for women, the onset of this condition occurs 7 to 10 years later. Nonetheless, it remains a leading cause of mortality for both sexes. For those aged 45 to 60, the incidence of IHD in men is 3 to 4 times greater than in women of the same age; however, by age 75, the incidence in women may surpass that in men. Unfortunately, the rates of morbidity, mortality, and disability from IHD continue to show a persistent trend of increase. According to Stamler, it has been noted that, "...IHD has become so prevalent that, if we do not change this trend, it will lead humanity to the greatest epidemic in the coming years." This underscores the need for ongoing research focused on identifying the causes of its occurrence and developing methods for preventing this disease.

IHD is characterized by myocardial damage caused by impaired blood flow through the coronary arteries (CAs), which can be either organic or functional. The concept of IHD includes both acute transient and chronic pathological conditions. The first description of classic angina pectoris belongs to Heberden (1772), who was the first to use the term "Angina pectoris." However, Hippocrates, as well as Bortalet (1576-1636), Harvey (1527-1658), and Morgani (1648-1771), described cases of severe, acute pain in the left side of the chest in elderly individuals, accompanied by anxiety, fear, shortness of breath, and fainting during attacks. Parry (1799) was the first to point out the relationship between angina and alterations in the heart's structure, along with damage to the coronary arteries. Many physicians, well before Heberden described comparable anginal episodes, emphasized their link to sudden cardiac death. Hippocrates remarked that, "...pain in the heart area, which appears with some regularity in people, is a sign of impending sudden death..." The term "acute coronary syndrome" (ACS) is used to denote the exacerbation of IHD. This term encompasses clinical conditions such as acute myocardial infarction (AMI) with ST-segment elevation (STEMI), AMI with ST-segment depression (NSTEMI), and unstable angina (UA). The

average incidence of ACS per year is about 520,000 cases, of which 36.4% are attributed to AMI and 63.6% to UA.

Assessing prognosis is a vital component in the treatment of patients with coronary heart disease (CHD). Traditional risk factors (RF) for the development of IHD, including family history, sedentary lifestyle, arterial hypertension (AH), smoking, dyslipidemia (DLP), obesity, and diabetes mellitus (DM), negatively affect the prognosis of patients already diagnosed with IHD, mainly due to their role in the progression of atherosclerosis. Additionally, there is evidence indicating that an elevated resting heart rate (HR) also has a detrimental effect on prognosis.

In general, the prognosis is less favorable in patients with reduced left ventricular ejection fraction (LVEF) and chronic heart failure (CHF), those with a higher number of affected vessels, more proximal stenosis, greater severity of coronary artery disease, more pronounced myocardial ischemia, younger patients, and those with more severe angina.

Currently, risk factors (RF) for ischemic heart disease (IHD) have been studied, among which arterial hypertension (AH), dyslipidemia (DLP), and smoking are of significant importance. However, in 50% of cases, IHD develops in individuals without lipid metabolism disorders. Frequently, pronounced atherosclerosis is found in the absence of RF, and their presence does not necessarily indicate its development.

In the diagnosis of atherosclerosis, the determination of biological markers and instrumental methods have found wide application. The disadvantages of using biochemical, physiological, instrumental, behavioral, and other indicators to identify the risk of IHD include their high lability, late ontogenetic penetrance, low specificity, and significant dependence on external environmental factors.

Prognosis assessment is an extremely important aspect of treating patients with IHD, allowing the physician to choose the appropriate management strategy. Therefore, the search for factors associated with the prognosis of patients with unstable IHD, as well as ways to influence these factors, remains relevant. Moreover, there are a number of patients for whom myocardial revascularization is not possible, and pharmacological therapy is insufficiently effective; thus, the development of additional treatment methods is a crucial issue.

Regrettably, individuals under the age of 45 are infrequently represented in research studies, even though their numbers in the population are on the rise. At present, there are only a few studies in our country that examine the prevalence of cardiovascular diseases (CVD) among younger individuals, and the prognosis for this demographic is not well understood, despite its significant relevance. To establish and execute effective preventive strategies, it is crucial to collect data on the risk factors (RF) that shape the epidemiological context of CVD, as these are among the most prevalent and serious health conditions. Nevertheless, there is no doubt that timely identification and correction of RF in young patients with IHD will significantly reduce loss of working capacity and mortality, which underscores the relevance of this research.

The development of domestic healthcare encompasses targeted measures aimed at improving the outcomes of early diagnosis of cardiovascular diseases (CVD), as well as the implementation of modern technologies for their prevention and treatment. Efforts

are being made to align the medical system with the requirements of global healthcare standards, including comprehensive regular screenings to identify risk factors (RF) for the development of CVD in the population. In this context, the timely identification of RF that contribute to the early development of CVD in young individuals is one of the pressing tasks of modern cardiology. This focus facilitates the implementation of early preventive measures and the individualized selection of corrective interventions.

CHAPTER 1
Literature review

Modern Perspectives on the Development of Coronary Artery Disease in Young Age

Currently, cardiovascular diseases (CVD) pose a significant issue in both global and national healthcare systems. Among these, diseases of the circulatory system (DCS), especially coronary artery disease (CAD), are the leading contributors to disability and mortality rates within the population. The World Health Organization (WHO) reports that DCS has emerged as the foremost cause of death in recent decades, accounting for one-third of all fatalities. Around 126 million people globally are diagnosed with CAD, leading to approximately 9 million deaths each year. CAD constitutes about one-third of all deaths in both economically developed and developing countries.

In 2018, the prevalence of coronary artery disease (CAD) in the United Kingdom was approximately 3.5% among men aged 30 to 45, which is four times lower than that of individuals over 75. A similar pattern was observed for women, with the prevalence in the older age group being five times higher. In the United States, newly diagnosed cases of CAD are projected to increase by an average of 26%. The prevalence of CAD rises progressively with age; for instance, in the U.S., among individuals aged 40 to 59, the rates were 3.3% for men and 1.8% for women. In the 60 to 79 age group, these figures rose to 11.3% for men and 4.2% for women. Specifically, the prevalence of CAD was 27.6% among men aged 40 to 50 and 20.4% among women aged 45 to 59. In the 60 to 69 age group, the prevalence reached 34.5%, while in the 70 to 79 age group, it was 37.7%. Importantly, the prevalence of CAD in individuals under 45 is expected to remain high by 2040.

In the last two decades, Uzbekistan has seen a significant increase in morbidity and mortality from DCS, with statistics reflecting global trends. According to the State Statistics Committee of the Republic of Uzbekistan, in 2020, the adult mortality rate increased by 13.5% compared to 2019, totaling 175,600 people, with 60% of deaths attributed to CVD. By 2030, the prevalence of CAD may increase by 18% compared to 2013, with mortality potentially reaching around 23.6 million people. Direct medical costs could nearly double compared to 2010. In all countries, including Uzbekistan, there is a trend toward younger patients with CAD, and various population groups are being affected. This highlights the need for early diagnosis and preventive measures, especially among the youth.

Recently, researchers have been actively investigating the features related to the onset and progression of coronary artery disease (CAD), especially its acute manifestations, in diverse patient groups differentiated by gender, age, comorbidities, and other relevant factors. The results obtained allow for a reassessment of traditional views. For a long time, it was believed that CAD was very common among the middle-aged and elderly population; however, it is now being observed more frequently in

individuals under 45 years of age. This change can be attributed to shifts in the lifestyle of young individuals, including increased sedentary behavior and a higher consumption of easily digestible carbohydrates and trans fats. These habits are associated with the development of dyslipidemia, obesity, and diabetes. Additionally, young people often engage in extra and overtime work, leading to a faster pace of life. They are frequently exposed to chronic stress, which in some cases results in smoking, alcohol consumption, energy drink intake, and overeating. The group at high risk for early development of CAD primarily includes young male smokers, individuals with a hereditary predisposition to early cardiovascular pathology, and those facing employment issues.

The clinical course of coronary artery disease (CAD) in young age is variable, and the disease can debut as acute coronary syndrome (ACS) (NSTEMI and STEMI) or sometimes the first (and probably the last) manifestation of CAD is sudden cardiac death. One of the features of CAD in young patients is the prolonged subclinical course of coronary pathology, with CAD debuting as STEMI. However, CAD often immediately takes on the character of a chronic disease, clinically manifesting as stable angina (SA) on exertion. The remaining cases statistically account for sudden and non-sudden cardiac death and acute coronary insufficiency.

The most typical manifestation of chronic CAD is SA on exertion. The presence of angina is established purely clinically. A detailed and competent inquiry of the patient allows clarifying the conditions, frequency, and nature of the pain sensations that arise, thus differentiating an angina attack from other chest pains (thoracalgias). The basis of any angina attack lies in temporary (transient) myocardial ischemia – a pathological condition that occurs when there is a mismatch between the myocardial oxygen demand and its delivery through occluded or spastic coronary arteries under increased load on the heart. Angina itself, as a syndrome, has unfavorable prognostic significance, and this significance is considered higher in men than in women.

The group at high risk for the early onset of coronary artery disease (CAD) mainly includes young male smokers, individuals with a genetic predisposition to early cardiovascular conditions, and those facing employment challenges.

In younger patients, the clinical course of CAD can be quite variable. The disease may begin as an acute coronary syndrome (ACS), such as NSTEMI or STEMI. In certain instances, the first—and potentially the only—indication of CAD could be sudden cardiac death.

Myocarditis can mimic AMI, which is a common diagnostic problem in young patients. The frequency of myocarditis among young patients diagnosed with AMI and having normal coronary arteries ranges from 33% to 70%.

Coronary artery disease (CAD) has a significant impact on disability and mortality among young people, making it a critical socio-medical concern. Over 75% of deaths due to cardiovascular diseases occur in low- and middle-income countries. Despite progress in the prevention and treatment of CAD, this condition remains a leading cause of morbidity.

Given the unique characteristics of CAD in younger individuals, it is essential to establish a comprehensive methodological approach to organizing medical care aimed at enhancing the diagnosis and treatment for this patient demographic.

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The risk factors for the development of CHD in young people

The rising prevalence of coronary artery disease (CAD) is linked to age-related changes in the cardiovascular system (CVS) as well as an increase in risk factors (RFs). Research in 2018 indicated that young men have lower rates of hypertension (HT) and diabetes mellitus (DM) compared to middle-aged men, yet they exhibit higher rates of obesity, smoking, and dyslipidemia. Therefore, a key focus in cardiology is not only identifying specific etiological RFs for the onset and progression of coronary atherosclerosis but also evaluating how these RFs contribute to morbidity and mortality from CAD across different age groups, especially among the youth.

Many researchers attribute the increase in CAD prevalence to the growing number of RFs, leading to the accumulation of multiple RFs in individual patients. Among individuals hospitalized for CAD aged over 40, it was found that 90.7% of men and 92.3% of women had at least one RF, while 69.9% of men and 70.1% of women had two or more RFs. Furthermore, 37.5% of men and 38.0% of women had three or more RFs. The presence of two or more RFs significantly heightened the risk of morbidity and mortality from CAD, and it has been noted that the combination of two to three RFs greatly increases the risk of mortality.

Risk factors for CAD can be categorized into non-modifiable and modifiable groups. Modifiable RFs include hypertension, hypercholesterolemia, diabetes mellitus, abdominal obesity, alcohol consumption, and a sedentary lifestyle. Non-modifiable RFs encompass age, male sex, and family history of cardiovascular diseases (CVD). In the Russian Federation, the ESSENCE-RF study (Epidemiology of CVD and their RFs in the regions of the Russian Federation), conducted from 2018 to 2021 across 11 regions, revealed that the prevalence of elevated blood pressure among individuals aged 20-44 was 57.4%, elevated cholesterol levels were at 74.5%, smoking rates stood at 15.3%, and obesity affected 46.9% of this population. Notably, the rates of elevated blood pressure and smoking were slightly higher in men, whereas the prevalence of hypercholesterolemia and obesity was greater among women.

Multivessel coronary artery disease (CAD) is more frequently observed in young patients with diabetes mellitus (DM) and multiple risk factors (RFs) that contribute to the progression of atherosclerosis. A study by G. Berenson and colleagues examined the relationship between the severity of atherosclerotic lesions and the number of RFs, including body mass index, systolic and diastolic blood pressure, total cholesterol levels, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and smoking. The data were collected from autopsies of 204 young individuals aged 2 to 39 who died from various causes, primarily injuries.

The results indicated that as the number of RFs increased, the severity of atherosclerotic lesions in young individuals also increased. Specifically, in individuals with 0, 1, 2, and 3 or 4 RFs, the coverage of fatty streaks in the aorta was 19.1%, 30.3%, 37.9%, and 35% of the intimal surface, respectively ($p=0.04$). For fatty streaks in coronary arteries, the figures were 1.3%, 2.5%, 7.9%, and 11% ($p=0.01$). Regarding atherosclerotic plaques in coronary arteries, the prevalence was 0.6%, 0.7%, 2.4%, and 7.2%, respectively ($p=0.003$)

It is important to note that age can amplify the impact of many modifiable risk factors (RFs). Research has shown that elevated cholesterol levels and blood pressure (BP) in men aged 35-44 years can increase the risk of coronary events by up to 15%. In the 45-64 age group, this risk rises to 15-30%, and for those over 65 years, it reaches 30% [20, 21].

According to a study by N.K. Wenger, atherosclerotic lesions in the coronary arteries (CA) were found in 5% of men aged 29-39 years, while in women, such lesions were detected at a rate ten times lower. In the age range of 39-49 years, the incidence of atherosclerosis in the male population was three times higher than in the female population. Men have more pronounced atherosclerotic changes in the CA, making them more susceptible to coronary artery disease (CAD) at any age. With age, the degree and frequency of atherosclerotic lesions of the CA increase. However, the contribution of

with age has remained consistent regardless of the study timeframe. For instance, between 2017 and 2019, 41.9% of men aged 25–34 were smokers, while the rate among those aged 55–64 had already dropped to 32.5% [38].

A similar age-related pattern is observed among individuals diagnosed with coronary artery disease (CAD). As the general population ages, not only does the overall smoking prevalence decline, but smoking frequency among CAD patients also diminishes. Research shows that among male CAD patients aged 56–65, 39.8% were smokers, whereas 38.9% of female patients in the same age group smoked. Among CAD patients over the age of 75, smoking rates fell to 11.8% in men and 7.9% in women [39].

Moreover, modifiable RFs often decreases with age. The prevalence of RFs among individuals suffering from cardiovascular diseases (CVD), including CAD, changes with age.

Arterial hypertension (AH) is a significant risk factor (RF) for the development of cardiovascular diseases (CVD), including coronary artery disease (CAD). It is well recognized that the prevalence of AH increases with age. In the USA, from 2017 to 2022, the prevalence in the age group of 40-54 years was 36.8% among men and 32.7% among women; in the 55-64 age category, it was 54.6% for men and 53.7% for women; in the 65-74 age group, the rates were 62% for men and 67.8% for women; and for those older than 75 years, it reached 76.4% for men and 79.9% for women. However, due to preventive and therapeutic measures, the USA has observed a decrease in average systolic blood pressure (BP) values from 130.5 mmHg to 128.1 mmHg among men and from 127.2 mmHg to 124.4 mmHg among women, alongside a reduction in age-standardized prevalence from 4% to 29% among men and from 25% to 20% among women.

In recent decades, the prevalence of AH in the Russian Federation has slightly increased. In 2013, the proportion of individuals with AH was 39.5%, while in 2020-2022, according to the ESSE study, the prevalence reached 44%, with 48.2% among men and 40.8% among women. In the 45-64 age group, the prevalence of AH was 74.5%. At the same time, among individuals older than young age, grade 3 AH was diagnosed more frequently compared to grades 1 and 2. An increase in systolic BP (SBP) >140 mmHg or diastolic BP (DBP) >94 mmHg doubled the risk of acute myocardial infarction (AMI) [33, 34]. A meta-analysis conducted in 2019 found that elevated

systolic blood pressure (SBP) in individuals over 40 was associated with unstable angina (UA) and acute myocardial infarction (AMI) [35]. Many researchers agree that arterial hypertension (AH) should not be regarded as an independent risk factor (RF) but rather as part of a broader risk assessment. In 2020, it was noted that around 40% of coronary events occurred in men and 68% in women with AH who also had two or more additional RFs [36].

Thanks to global anti-smoking initiatives, the overall prevalence of smoking has declined over the past decades. In the United States, for example, smoking rates dropped to 17.9% over a 15-year period. As of 2018, 20.4% of men aged 18 and older reported smoking, compared to 15.5% of women in the same age group.

In younger men aged 18 to 44, smoking prevalence decreased from 27.9% in 2019 to 22.9%. A similar downward trend was seen among women in this age group. However, despite these improvements, approximately 2.3 million individuals over the age of 16 started smoking for the first time in 2018, including 1.1 million adults aged 18 and above.

Smoking rates tend to decline with age. Among individuals aged 65 to 74, the smoking rate was 13.4%, and it dropped further to 8.2% among those aged 75 and older. At the same time, the percentage of people who quit smoking increased slightly—by only 1.4%—reaching 24.4% in the elderly population.

In Russia, the prevalence of smoking among men declined by 20.8% over two decades, reaching 39% by 2018. In contrast, the percentage of women who smoke increased from 9.1% in 1993 to 13.6% during the 2018–2022 period. Interestingly, the trend of decreasing smoking rates statistically significant associations have been found between smoking intensity and the presence of CAD in men. As the disease advances, the proportion of men who engage in low-intensity smoking increases compared to those without CAD—23.1% versus 10.3%, respectively. However, the proportion of male CAD patients who smoke heavily remains at 15.4%, while the rate for women is slightly lower at 11.1% [40].

Comparable results were observed when examining the impact of smoking on cardiovascular-related mortality. The risk of death from cardiovascular causes was found to be 2.07 times higher among current smokers and 1.37 times higher among former smokers. A clear dose-response relationship was noted, with each additional 10 cigarettes smoked daily increasing the mortality risk by approximately 1.4 times [41].

Quitting smoking has been consistently associated with lower mortality, even in individuals diagnosed with coronary artery disease (CAD). A 2019 meta-analysis demonstrated that CAD patients who stopped smoking experienced a 36% reduction in relative mortality risk compared to those who continued smoking. This benefit was observed across all age groups and in both men and women [42].

Therefore, smoking cessation remains a critical health recommendation at any age. It is essential to recognize that smoking exerts a cumulative effect by intensifying the impact of other cardiovascular risk factors, such as elevated cholesterol and high blood pressure. For example, the mortality risk in smokers with both high systolic blood pressure and increased cholesterol levels is twice as high as that in non-smokers with the same clinical profile.

Dyslipidemia—marked by elevated total cholesterol, triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C), along with reduced levels of high-density lipoprotein cholesterol (HDL-C)—is a significant risk factor for the onset of coronary artery disease (CAD). It is well established that aging is associated with increasing levels of cholesterol, TG, and LDL-C, while HDL-C tends to decline. Data from the National Health and Nutrition Examination Survey (NHANES) indicate that elevated LDL-C was present in 11.7% of individuals aged 20–39, compared to 41.2% in those aged 40–64 [58].

Findings from the Framingham Heart Study confirm a strong link between aging and rising plasma LDL-C concentrations. From age 20 onward, LDL-C levels in men increase more rapidly than in women. However, postmenopausal women experience a pronounced rise in LDL-C levels, while men between 40 and 60 years old show relatively stable concentrations. Consequently, women in this age range tend to have higher LDL-C levels than their male counterparts. Regarding triglycerides, levels in men typically rise until around age 40–50, after which they begin to decline, whereas in women, TG levels continue to climb with age.

It's important to note that the observed reduction in lipid levels among older adults often reflects the "survival effect." This phenomenon refers to the earlier mortality of individuals with poor cardiovascular profiles—such as those with high cholesterol—which skews the data in older populations. For example, a 10% reduction in cholesterol levels in 40-year-old men correlates with a 54% reduction in cardiovascular risk. In contrast, the same cholesterol reduction in 70-year-old individuals results in only a 20% risk reduction [22].

The prevalence of hypercholesterolemia (defined as cholesterol levels ≥5.0 mmol/L) was slightly lower among men aged 40–59. However, obesity and arterial hypertension (AH) were more commonly observed in older men, with rates of 41.5% and 21.7%, respectively [23].

According to the ESSE study, conducted across 11 regions in Russia, 58.1% of men were found to have hypercholesterolemia. Among those aged 45–54, the rate increased to 66.4%. In women, the prevalence of elevated cholesterol levels rose steadily with age—reaching 71.1% in the 45–54 age group and 78.8% among those aged 55–64. Similar age-related increases were observed for elevated LDL-C and triglycerides. In the 45–64 age group, 33.9% of individuals had hypertriglyceridemia, while elevated LDL-C levels were noted in 74.5% [60].

The risk of mortality from coronary artery disease (CAD) rises significantly when hypercholesterolemia is present alongside other risk factors. Research indicates that individuals suffering from both high cholesterol and hypertension are at a considerably greater risk of fatal CAD events [19]. These findings support the concept of cumulative cardiovascular risk and have contributed to the development of assessment tools such as the SCORE (Systematic Coronary Risk Evaluation) system. SCORE is designed to estimate the 10-year risk of cardiovascular death based on key factors including sex, age, systolic blood pressure, total cholesterol levels, and smoking status [63].

In patients with CAD, even mild lipid abnormalities should be addressed. Statin therapy is commonly employed for this purpose, as these drugs effectively lower LDL-C concentrations by 22% to 60%, depending on dosage.

Obesity represents another major contributor to cardiovascular risk and is closely associated with hypertension, elevated cholesterol, and type 2 diabetes. Its prevalence increases with age, reaching a peak between 45 and 69 years, while the lowest obesity rates are found among individuals aged 20–40 [66]. This age-related pattern of obesity has remained relatively stable throughout the 20th century, although the prevalence within these age brackets has gradually risen over time.

7.8 liters among women. In comparison, consumption levels in Germany were Consequently, it can be inferred that preventive strategies targeting risk factors like obesity have not been sufficiently effective. Projections suggest that the incidence of CAD could rise by 5% to 16% solely due to escalating obesity rates [67]. In Russia, obesity trends reflect global patterns. The lowest prevalence is seen in 20-year-olds, while the highest is observed around age 60. Among women, obesity was 2.5% more common than among men, with approximately 23.2% of women classified as obese compared to 8.7% of men.

A similar age-related pattern applies to abdominal obesity. Among men, the rate increases steadily with age—from just 1.5% at age 20 to 20.9% in those aged 80 and above. In women, abdominal obesity also rises with age, peaking between 40 and 60 years before declining slightly in older age groups. Nevertheless, abdominal obesity is markedly more prevalent in women than in men [68].

Previous research has established strong links between obesity and various forms of cardiovascular disease (CVD), including angina pectoris (AP), acute myocardial infarction (AMI), heart failure, and sudden cardiac death [69–71]. Some scholars suggest that the increased risk of cardiovascular events in obese individuals may be explained by endothelial dysfunction and low-grade inflammation of the vascular walls [72]. Additionally, obesity has been consistently associated with higher mortality risk. Interestingly, many studies report what is known as the “obesity paradox”—a U-shaped curve indicating that both low and high body mass index (BMI) values are linked to increased mortality.

Alcohol Consumption

A considerable number of epidemiological studies have revealed a protective association between moderate alcohol intake and a reduced risk of coronary artery disease (CAD) [43]. This effect is believed to stem from alcohol’s influence on several pathogenic mechanisms that contribute to CAD. Moderate alcohol consumption is known to reduce chronic inflammation and promote vasodilation [44]. It also positively impacts lipid metabolism by enhancing HDL-C levels and lowering LDL-C concentrations, thereby reducing the prevalence of hypercholesterolemia [45–47].

Moreover, alcohol can help lower blood glucose levels by inhibiting hepatic gluconeogenesis, which may subsequently reduce the occurrence of hyperglycemia and hyperinsulinemia—both recognized risk factors for CAD [48–50]. Small quantities of alcohol also contribute to reduced fibrinogen levels and inhibit platelet aggregation, thus supporting vascular health [51].

Mukamal K.J. et al. demonstrated that regular alcohol consumption significantly lowers the risk of CAD in individuals aged 65 and older. In those with subclinical CVD and those without any history of CVD, consuming 14 grams or more of alcohol per week was associated with hazard ratios of 0.52 (95% CI: 0.35–0.79) and 0.44 (95% CI: 0.19–0.99), respectively [52].

In another study focused on older adults, Sacco P. et al. identified smoking and depression as risk factors for excessive alcohol use, while being female, of advanced age, or having a higher education level were all associated with a decreased risk of alcohol dependence [56]. According to WHO statistics, between 2008 and 2010, the average annual alcohol consumption per capita in Russia was 23.9 liters among men and 16.8 liters for men and 7.0 liters for women [57].

Diabetes mellitus (DM) in young patients with coronary artery disease (CAD) is less common; however, individuals with type 2 diabetes have a 2- to 6-fold higher risk of cardiovascular disease (CVD) mortality, with the disease progressing faster and at an earlier age compared to those without this condition [42]. Hyperinsulinemia enhances lipolysis, increases levels of free fatty acids, very-low-density lipoproteins (VLDL), triglycerides (TG), and low-density lipoproteins (LDL) [6, 16], increases platelet and monocyte adhesion, and stimulates the secretion of thromboxane A2 and platelet-derived growth factor, leading to damage of atherosclerotic plaques (ASP) and endothelial dysfunction. In dyslipidemia, smooth muscle cells can absorb modified LDL and transform into foam cells, contributing to atherogenesis [32].

A significant proportion of young patients with coronary artery disease (CAD) report a family history of cardiovascular disease (CVD), with estimates ranging from 41% to 64% of cases [2]. According to findings from the Framingham Heart Study, the presence of clinically confirmed CVD due to atherosclerotic changes in a parent or sibling doubles an individual’s risk of developing CVD, irrespective of other conventional risk factors [13, 29]. Genetic predisposition also encompasses metabolic disorders, including abnormalities in lipid and carbohydrate metabolism, coagulation system dysfunctions [32], and an elevated risk of early-onset conditions such as hypertension, stroke, and type 2 diabetes mellitus [15, 18]. Despite these associations, the exact biological mechanisms through which CVD is inherited remain not fully understood.

Psychological stress is another well-recognized factor contributing to the development of CVD. In Europe, stress-related cardiovascular conditions are reported in approximately 25% to 33% of cases, while in Russia, this figure stands at 19.3% [48]. Elevated occupational stress, emotional pressure, irregular work hours, and disturbances in sleep patterns often lead to anxiety and depressive disorders, which are closely linked to a higher incidence of cardiovascular complications and increased mortality risk [2, 18].

A significant negative aspect of psycho-emotional stress is its reinforcement of various harmful behavioral patterns, such as alcohol consumption, smoking, excessive intake of simple carbohydrates, and physical inactivity [48].

An ***unhealthy diet*** characterized by excessive consumption of high-fat foods and insufficient intake of fruits and vegetables (less than three servings per day) is one of

the major RFs for CVD [7, 9, 10, 37]. The consumption of processed foods, sugary carbonated beverages, and refined carbohydrates leads to weight gain and obesity, which in turn contribute to the development of hypertension, type 2 DM, and atherosclerotic vascular lesions [37]. Avoiding cholesterol-rich foods and incorporating fiber-rich foods, particularly leafy vegetables and fruits, into the diet helps normalize carbohydrate and lipid metabolism and improve overall homeostasis [22, 23].

Currently, it is well established that CVDs are multifactorial in nature. In clinical practice, it is rare to encounter a patient with a single RF. Moreover, RFs act synergistically, amplifying each other's negative effects, and the cumulative risk in such cases exceeds the sum of individual risk components. Therefore, even if each RF is only moderately elevated, the overall risk of CVD in a patient may still be high due to the interplay of multiple factors. This highlights the importance of considering all major risk factors and their combined contribution when assessing an individual's likelihood of developing CVD.

Although the causes and clinical presentations of coronary artery disease (CAD) in young patients vary widely, the course of the disease remains highly individual. Gaining deeper insight into the etiopathogenetic mechanisms, clinical features, hemodynamic parameters, and the extent and severity of atherosclerotic involvement in the coronary arteries is essential for tailoring personalized treatment strategies and reducing the risk of complications.

Thus, studying the living conditions, work environments, and health status of young individuals, as well as identifying adaptation mechanisms to changing environments, is a pressing issue related to preserving the intellectual potential of the country. Given the above, investigating RFs for the development of cardiovascular pathology in young people remains highly relevant.

Modern concepts and clinical features of the course of CHD in young people.

Although the causes and clinical presentations of coronary artery disease (CAD) in young patients vary widely, the course of the disease remains highly individual. Gaining deeper insight into the etiopathogenetic mechanisms, clinical features, hemodynamic parameters, and the extent and severity of atherosclerotic involvement in the coronary arteries is essential for tailoring personalized treatment strategies and reducing the risk of complications.

Excessive physical activity immediately preceding the onset of chest pain was more frequently observed in men (7 out of 16 cases) compared to women (2 out of 71 cases), with the difference reaching statistical significance ($p < 0.001$). Among female patients, 13 (18%) were in the postpartum period at the time of presentation. Additionally, fibromuscular dysplasia of the iliac arteries was identified in 8 (50%) out of 16 women who underwent femoral artery coronary angiography (CAG). In 49% of all cases, patients presented with ST-segment elevation myocardial infarction (STEMI). Percutaneous coronary intervention (PCI) was successfully performed in 28 (65%) of 43 patients. However, complications occurred in 7 cases due to the extension of dissection or intramural hematoma, which necessitated the placement of more than two

stents. In other cases, PCI failed due to technical complications such as the coronary guidewire entering a false lumen or exacerbating the dissection and hematoma, leading to complete vessel occlusion [66].

Two separate investigations involving over 100 pregnant women each examined the underlying causes of acute myocardial infarction (AMI) using coronary angiography or autopsy data. One study involving 103 pregnant patients revealed that coronary atherosclerosis was present in only 40% of cases. The remaining cases were attributed to coronary artery (CA) dissection (27%), thrombosis in angiographically normal arteries (8%), CA spasm (2%), and coronary embolism (2%), while 13% of cases remained etiologically unclear [67]. In another study involving 129 women, coronary atherosclerosis accounted for 27% of AMI cases, while other causes included CA dissection (43%), thrombosis without underlying atherosclerosis (17%), CA spasm (2%), Takotsubo cardiomyopathy (1.5%), and unknown factors in 9.5% of patients [68].

Less common etiologies of CAD in younger individuals include coronary artery spasm, triggered either by endogenous factors (vasospastic angina) or external vasoconstrictive substances such as cocaine or methamphetamines [69]; nonspecific aortoarteritis (Takayasu arteritis), which occurs in 2–3 per 100,000 individuals—predominantly in women under 40 (male-to-female ratio 1:9)—and can manifest as severe recurrent large-focal AMI when the coronary arteries are affected [70, 71]; blunt chest trauma leading to coronary thrombosis or dissection [72]; extreme physical exertion resulting in focal myocardial injury; toxic exposures (e.g., lead, alcohol, illuminating gas, disulfiram); pheochromocytoma; and hypothyroidism [54, 70, 73, 74].

When discussing the characteristics of myocardial infarction (MI) in young individuals, it is important to remember that, in most cases, it develops against a background of relative health, with more or less normal blood circulation in the coronary vessels and arteries. Changes and disturbances in coronary artery blood flow, as well as the development of occlusion, occur in the absence of a well-developed collateral circulation, intra- and intercoronary arcades, and anastomoses that could at least partially compensate for impaired blood flow at this age [1, 3]. The literature contains limited data on the development of acute myocardial infarction (AMI) in young individuals [5, 6].

The possible causes of AMI in young patients include:

1. Atherosclerotic lesions of the coronary arteries (CAs);
2. Coagulation system disorders leading to thrombosis and thromboembolism of coronary vessels;
3. Vasoregulatory disturbances in coronary blood flow resulting in CA spasm;
4. Infectious-allergic or toxic damage to the CAs with subsequent fibrosis;
5. Non-inflammatory arteriopathy;
6. Congenital anomalies of major CAs;
7. Idiopathic CA dissection.

The clinical course and presentation of CAD in young individuals are highly variable. The disease may debut as an acute coronary syndrome (ACS), including unstable angina or AMI, while in some cases, the first manifestation of CAD is sudden

cardiac death. However, CAD often progresses directly into a chronic condition, clinically presenting as stable or unstable exertional angina.

Thus, studying the significant risk factors associated with the early development of CAD in young patients will enhance the understanding of its causes, progression, and clinical features. This knowledge is crucial for improving early diagnosis, treatment strategies, and the development and implementation of preventive programs for this patient group. These findings further emphasize the need for a unified approach to the early diagnosis, treatment, and prevention of CAD in young men.

Modern possibilities of risk stratification and prediction of adverse outcomes in patients with CHD

Despite the significant achievements in the diagnosis, treatment, and prevention of this disease, IHD remains one of the most pressing issues in modern cardiology and public health as a whole [1]. The primary cause of hospitalizations in IHD is the development of ACS. After establishing the diagnosis of IHD, determining the patient's prognosis becomes the most important task. Risk stratification for the development of complications in patients with IHD is necessary to determine treatment tactics, hospitalization timing, and the development of individualized rehabilitation programs and secondary prevention [2]. Patients with IHD have an increased risk of developing adverse cardiovascular events, such as AMI, stroke, recurrence of angina attacks, and cardiac death both during hospitalization and thereafter.

Risk stratification in IHD is imperfect; consequently, there is a need to search for new markers, including laboratory ones, and to clarify the role of known markers that have high prognostic value with regard to the development of unstable and stable angina, the course of the disease, and monitoring the outcomes of pharmacological therapy in patients with IHD [3]. To improve risk stratification, the use of biomarkers reflecting various pathophysiological processes is possible [4].

Despite continuous advancements in healthcare, identifying the factors contributing to post-discharge complications in patients with ischemic heart disease (IHD) remains a pressing clinical issue.

Extensive literature has been devoted to analyzing the influence of various determinants on the prognosis of individuals with IHD [19, 119, 130, 154]. However, focusing on a single prognostic factor is no longer considered sufficient. The most informative variables, frequently included in prognostic models, encompass demographic factors (such as sex and age), clinical parameters (systolic blood pressure, heart rate), electrocardiographic findings (location and degree of ST-segment deviation), myocardial systolic function, the extent and nature of coronary artery involvement, medical history (including post-infarction cardiosclerosis, sudden cardiac death, and obesity), as well as laboratory markers (myocardial necrosis indicators, markers of systemic inflammation, creatinine clearance, glycemic status), and the severity of atherosclerotic lesions in coronary arteries [35, 106, 125, 110].

With the current development of medical technologies, electronic risk calculators and mobile applications have been introduced to facilitate the use of various clinical risk assessment tools in patients with IHD [1]. One of the most widely adopted tools for

estimating long-term adverse outcomes in patients with acute myocardial infarction (AMI) is the GRACE (Global Registry of Acute Coronary Events) score [154]. Developed from data on 43,810 individuals enrolled in the GRACE and GUSTO studies, the GRACE score exhibits high sensitivity and specificity for predicting adverse events and is strongly supported by evidence. It has been endorsed for clinical application by the European Society of Cardiology (2017) [191].

However, some studies have raised concerns regarding the limited prognostic accuracy of the GRACE score in patients following percutaneous coronary intervention (PCI). Certain authors suggest that integrating angiographic data with specific clinical, ECG, and laboratory findings can lead to the development of enhanced prognostic models with superior predictive value compared to the GRACE score [85].

For asymptomatic patients with cardiovascular risk factors, the Systematic Coronary Risk Evaluation (SCORE) algorithm assesses the individual 10-year risk of cardiovascular events in order to initiate primary prevention, such as lifestyle changes and possible pharmacological therapy [25]. Patients with symptoms, on the contrary, require pharmacological therapy to reduce the clinical presentation of angina and/or improve the prognosis, including lifestyle changes, optimal pharmacological therapy, and ultimately, revascularization therapy.

The prognosis for symptomatic patients with confirmed stable IHD, recently redefined as chronic coronary syndrome (CCS), has improved in recent years thanks to innovations in pharmacotherapy and revascularization methods. In the Russian Federation, from 2004 to 2014, the number of percutaneous coronary interventions (PCI) increased more than 10 times and the number of coronary artery bypass grafting (CABG) operations tripled (from 10,419 to 30,191) [26, 27]. In part, thanks to the development and availability of different myocardial revascularization methods, mortality rates have decreased; however, the standardized mortality rate from myocardial infarction in the Russian Federation in 2014 was 35.4 cases per 100,000 population, and survivors still face a high risk of recurrent cardiovascular events [28]. Nevertheless, CHD remains the main cause of death among Russians – nearly half (47%) of all deaths. The annual mortality rate from IHD among the population of Russia is 27%. It is also important that 42% of all those who die from IHD die at working age. Patients diagnosed with stable angina die from IHD twice as often as those without this condition [4, 5]. According to various registries, among all patients with IHD the annual overall mortality is 1.2–2.4%, fatal cardiovascular complications (CVC) cause death in 0.6–1.4% of patients annually, and non-fatal myocardial infarctions occur at a frequency of 0.6–2.7% per year [4, 5, 29, 30].

A substantial body of literature reflects ongoing efforts by researchers to enhance the predictive accuracy of existing cardiovascular risk assessment models by incorporating emerging prognostic factors—clinical, biochemical, and genetic in nature [167]. Nonetheless, within the framework of personalized medicine, forecasting adverse outcomes in ischemic heart disease (IHD) requires individualized patient profiling. It is well established that patients with IHD vary significantly by age in terms of cardiovascular risk factor profiles, comorbidity burden, gender distribution, frequency of ST-segment elevation myocardial infarction (STEMI), and the approach to

myocardial revascularization [141]. Consequently, the impact of certain prognostic indicators on post-discharge mortality is likely to differ substantially between younger and older cohorts.

This hypothesis is supported by a study conducted by Y. Plakht et al. (2015), which analyzed the long-term outcomes of 2,763 patients diagnosed with acute myocardial infarction (AMI). Over a 10-year follow-up period, distinct predictors of post-hospital mortality were identified for different age groups. In elderly patients, mortality was significantly associated with advanced age, left main coronary artery involvement, and neurological conditions. In contrast, younger patients (under 65 years) showed higher mortality risks associated with anemia, alcohol dependency, renal dysfunction, and prior myocardial infarction.

Although identifying adverse prognostic markers in young and middle-aged patients with IHD holds both clinical and scientific importance, relevant studies investigating clinical, laboratory, and instrumental risk factors in these populations remain relatively limited in Russian medical literature.

In the Russian Federation, some success has been achieved in the development of original models for predicting both short- and long-term outcomes in IHD patients [77]. Based on data from the RECORD-3 registry, the RECORD-6 risk scale was created to predict six-month mortality following hospital discharge after an episode of acute coronary syndrome (ACS). The RECORD-6 model identifies the following factors as predictors of mortality: lack of aspirin or beta-blocker prescription at discharge, new-onset heart failure during hospitalization, age over 75 years, body mass index ≤30 kg/m², serum creatinine levels ≥100 μmol/L on admission, and failure to perform urgent percutaneous coronary intervention (PCI). A cumulative score of 3 or more indicates a high mortality risk.

Furthermore, the “LIS” study [6] identified 15 prognostically significant variables for patients with AMI and introduced the LIS index—a scoring system designed to estimate the risk of adverse outcomes post-myocardial infarction.

Over the past decade, there has been growing interest in the use of hematological parameters to assess the severity of coronary atherosclerosis and stratify cardiovascular risk [202, 51, 108, 148, 142, 143]. Among these, the neutrophil-to-lymphocyte index (NLI)—defined as the ratio of absolute neutrophil count to lymphocyte count—has garnered considerable attention. The Jackson Heart Study found that an NLI exceeding 2.15 was independently associated with increased all-cause mortality (odds ratio [OR] = 1.40; 95% confidence interval [CI]: 1.14–1.70) and coronary heart disease (OR = 1.69; 95% CI: 1.23–2.34) [213]. Multiple studies have confirmed the correlation between NLI and the severity of coronary atherosclerosis in acute coronary syndrome (ACS), as well as its prognostic value in adverse post-AMI outcomes [135, 68, 88, 95, 213]. Notably, a study by Zhou D. et al. demonstrated that the inclusion of NLI in the GRACE (Global Registry of Acute Coronary Events) risk model significantly enhanced its predictive capability for adverse cardiovascular events in AMI patients.

Therefore, the clinical utility of hematological indices—particularly the NLI—for risk stratification in younger and middle-aged IHD patients appears promising.

Nevertheless, data regarding their prognostic relevance in these patient groups are almost entirely absent from the domestic literature currently available.

Innovative approach to therapy of patients with CHD in young men

Globally, more than 17 million individuals die annually from coronary heart disease (CHD), with ischemic heart disease (IHD) accounting for over half of these deaths. Of particular concern is the increasing prevalence of IHD among younger individuals—an age group that represents the core of the economically active population and significantly influences the socioeconomic development of nations [78]. Against the backdrop of this alarming trend toward earlier onset of IHD—often associated with a high incidence of fatal outcomes—one of the key priorities in contemporary healthcare is to identify the specific clinical features of the disease in younger populations and to address the modifiable risk factors contributing to its development [93, 71, 182].

Among the most critical risk factors implicated in the pathogenesis of atherosclerosis and its complications are disorders of lipid metabolism (dyslipidemia) and cytokine imbalance. These two factors should not be viewed in isolation, as their interplay significantly amplifies the risk and accelerates the progression of atherosclerotic disease. Understanding the combined role of these factors forms the foundation for both pharmacological and non-pharmacological therapeutic strategies aimed at the long-term management of affected individuals [90].

Currently, one of the most urgent challenges is the management of young IHD patients with coexisting dyslipidemia and cytokine imbalance using therapies that modulate both lipid profiles and inflammatory mediators. Despite the expanding arsenal of pharmaceutical agents targeting lipid and cytokine pathways, clinicians often face considerable difficulty in selecting the most appropriate drug regimen tailored to an individual patient's clinical profile [60, 70].

The overarching therapeutic objective in IHD management remains the enhancement of patient quality of life through the reduction of angina frequency, prevention of acute myocardial infarction (AMI), and improvement in survival outcomes—goals that align with contemporary, evidence-based clinical guidelines [71]. In addition to lifestyle modifications, the pharmacological management of IHD typically includes long-acting nitrates, β-blockers, calcium channel antagonists, antiplatelet agents such as acetylsalicylic acid or clopidogrel, and statins. Nevertheless, despite notable advancements in both preventive strategies and treatment modalities, the widespread adoption of interventional procedures (e.g., angioplasty, stent implantation, and coronary artery bypass grafting), as well as further optimization of drug therapy, continues to be an urgent focus within the field [78].

Among the medications, a particular interest is held by the complex drug of our domestic production (LLC "Temur Med Farm", Tashkent) Levocarnitine+L-arginine hydrochloride, which contains the amino acids levocarnitine and arginine hydrochloride. The influence of Levocarnitine+L-arginine hydrochloride on the clinical course of IHD with dyslipidemia and cytokine imbalance has been insufficiently studied and thus represents one of the challenges of modern cardiology.

Levocarnitine, which is a component of the Levocarnitine+L-arginine hydrochloride drug, performs the primary function of transporting fatty acids into the mitochondrial matrix through the inner membrane, which is crucial in the β-oxidation process for ATP production. In patients of any age suffering from myocardial ischemia, peripheral vascular diseases, chronic heart failure (CHF), dyslipidemia, and IHD, an absolute or relative deficiency of levocarnitine is observed [85]. The potentially positive effect of treatment with this drug lies in the fact that levocarnitine increases glucose metabolism by stimulating aerobic glycolysis, enhances coronary blood flow, and possesses antiarrhythmic and antioxidant effects [156]. Levocarnitine reduces the basal in occluded coronary arteries, which improves the clinical status of patients with ischemic heart disease (IHD). This leads to a reduction in angina attack frequency, a decreased need for nitrate use, improved exercise tolerance, and better rheological properties of blood. It also has an antithrombotic effect, significantly lowering the risk of thrombus formation and acute coronary syndromes (ACS) [119, 223].

L-arginine is also noted for its anti-hypoxic, cytoprotective, antioxidant, detoxifying, and membrane-stabilizing effects. As a nitric oxide (NO) donor, it participates in essential physiological processes related to cellular energy metabolism. L-arginine contributes metabolic rate in the body and slows down the breakdown of protein and carbohydrate molecules. It participates in the catabolism of long-chain fatty acids (such as palmitic acid and others) with the formation of acetyl-CoA, which is considered necessary in the gluconeogenesis process to ensure the activity of pyruvate carboxylase, and for the synthesis of choline and its esters. Under the influence of levocarnitine, ketone bodies are produced, and oxidative phosphorylation and the formation of adenosine triphosphate (ATP) occur. Additionally, levocarnitine facilitates the mobilization of fat from adipose tissue [69].

Levocarnitine enters the human body via two routes: through dietary products (meat products) and via endogenous synthesis in the kidneys and liver. Its elimination from the body occurs as a result of degradation by intestinal bacteria and filtration of the blood through the renal tubules. For this reason, a constant supply of levocarnitine should result from meat consumption (in 75% of cases) and its endogenous synthesis (in 25% of cases). Endogenous synthesis of levocarnitine is carried out using the essential amino acids lysine and methionine, which are obtained from food products, and also involves iron ions, vitamins C, B6, and niacin. The transport of water-soluble levocarnitine from the blood and extracellular fluid into the cells of the heart and coronary arteries occurs through the plasma membranes of these cells. In the mitochondria and cytoplasm of these cells, levocarnitine helps reduce the accumulation of long-chain fatty acids, thereby lowering the toxic effects of long-chain acyl-CoA in myocytes and coronary artery endothelium [145]. Levocarnitine acts as a cofactor controlling the rate of oxidation of long-chain fatty acids, facilitating their transport across the inner membrane, and also participates in removing their excess from the mitochondria and cytoplasm [62, 105].

Against the background of levocarnitine administration, the bioavailability of nitric oxide (NO) in the coronary vessels is optimized and systemic oxidative stress is reduced, which is the main mechanism in the comprehensive therapy of patients with

IHD and postinfarction cardiosclerosis (PICS) [11, 12]. Levocarnitine also improves the functioning of the reproductive system in males, enhances sperm quality, and normalizes testosterone hormone levels [8]. According to many studies, it has been found that during prolonged ischemia, the level of levocarnitine decreases in the ischemic and peri-ischemic zones. With the administration of levocarnitine, myocardial metabolism improves and ATP stores are preserved during ischemia, which positively affects the severity of ischemic and reperfusion injury of the heart muscle and reduces the necrosis zone [156, 217]. In a randomized, placebo-controlled study, it was noted that in 47 patients with stable angina, regardless of gender, the addition of levocarnitine at a daily dose of 2 g per os for 3 months in combination with conventional therapy significantly increased the duration of graded physical exertion and reduced the time for the ST segment on the ECG to return to its baseline after physical exertion compared to placebo [69, 217, 225].

The second active component of the combination therapy levocarnitine + L-arginine hydrochloride is L-arginine—an essential amino acid known for its beneficial effects on the cardiovascular system. L-arginine plays a crucial role in maintaining optimal blood cholesterol levels and significantly reduces adipose tissue accumulation. Moreover, it contributes to enhancing collateral circulation to reducing leukocyte and platelet activation, as well as their adhesion to vascular endothelium—mechanisms central to the prevention of ACS. Additionally, L-arginine is involved in fibrinolysis and plays a role in spermatogenesis [104, 224].

L-arginine hydrochloride performs vital functions in critical conditions, serving as a substrate for NO synthase—the enzyme responsible for NO production in endothelial cells—thereby helping to maintain vascular homeostasis and prevent ACS. Furthermore, it inhibits the synthesis of endothelin-1, a potent vasoconstrictor that promotes vascular smooth muscle cell proliferation and migration. Numerous studies have demonstrated that oral administration of L-arginine at a dose of 6 g/day significantly improves patients' quality of life, reduces nitroglycerin use, and, in some cases, leads to the complete resolution of anginal pain at rest [104, 105].

Thus, the current body of literature highlights the clinical importance of investigating the mechanisms underlying IHD in younger populations, particularly in men. Early identification of dyslipidemia and cytokine imbalance is essential for timely intervention. However, the effect of the combination drug levocarnitine + L-arginine hydrochloride on the clinical course of IHD in young men with concurrent dyslipidemia and cytokine imbalance remains inadequately studied. This gap underscores a pressing need for further research in this area. Early and targeted therapeutic strategies hold promise for preventing disease progression and improving overall outcomes and quality of life in this patient cohort

CHAPTER 2.
Results of domestic and international studies on the prevalence of risk factors in patients with unstable variants of angina among working-age individuals

Clinical features of the manifestation of CHD in young individuals

Cardiovascular diseases remain the leading cause of death globally, with ischemic heart disease (IHD) accounting for 25 to 50% of all cardiovascular deaths [221]. Additionally, the morbidity and mortality rates among the younger population, particularly individuals under 45 years of age, are increasing. Primary manifestations of atherosclerosis are now more frequently observed around the age of 20. Numerous studies have shown that the prevalence of IHD in men under 45 years is 1.4 to 1.5 times higher than in women of the same age [84].

The clinical presentation of IHD in younger individuals has distinct features. Young patients with complaints of substernal pain are less likely to seek medical attention compared to older individuals [152]. Moreover, in these patients, the medical history and characteristics of chest pain are often poor indicators of myocardial ischemia [195]. For many young men, the onset of IHD, particularly acute myocardial infarction (AMI), is preceded by a brief ischemic history. According to multiple international studies, only 24% of young men sought medical help due to intense anginal pain, and 69% had no prior history of angina [14, 41].

n most young patients, clinical symptoms persist for several days, with ischemic changes in the myocardium detectable on the electrocardiogram (ECG) immediately after the onset of the anginal episode. Atypical substernal pain in this population is often associated with coronary vasospasm, microcirculatory insufficiency of the coronary bed, or vegetovascular dystonia, rather than coronary artery stenosis [167]. A key characteristic of IHD in young patients is the heightened risk of recurrent AMI or sudden cardiac death.

The development of IHD in young individuals has several important features that are crucial for cardiologists during diagnosis. These include:

• The difficulty of early IHD diagnosis in the young, as they rarely seek medical attention for substernal pain due to underestimating their general condition and the relatively low degree of vigilance among physicians in such cases;

• In young individuals, the debut of IHD as AMI most often occurs during periods of intense physical exertion—intensive work, sports training and competitions, hiking, etc.;

• Pharmacological therapy for patients under 45 years with confirmed IHD is prescribed on general grounds [53];

• In the post-infarction period, young patients less frequently develop heart failure, recurrent infarctions, and postinfarction angina compared to older patients;

• For young individuals with confirmed or suspected IHD, targeted diagnostic methods, including coronary angiography (CAG), should be employed;

• If atherosclerotic lesions in the coronary arteries are identified, an active myocardial revascularization strategy should be pursued using balloon angioplasty or coronary artery bypass grafting (CABG);

• If signs of IHD are detected in young patients against a background of intact or minimally changed coronary arteries, active investigation should be conducted to identify systemic diseases and non-atherosclerotic coronary artery lesions.

Thus, utilizing data from the literature in clinical practice can aid in the early identification of patient groups at high risk for disease development. This, in turn, will enhance the quality of diagnosis, treatment, early prevention, and prognosis of cardiovascular complications.

Currently, cardiovascular diseases account for 25–50% of annual deaths worldwide, with ischemic heart disease (IHD) alone responsible for over 7 million deaths, constituting 12.8% of all cases [16, 59, 78]. Furthermore, morbidity and mortality rates are rising among young individuals, particularly affecting men. According to various studies, mortality in young men is 4.7 times higher compared to women of the same age, with mortality from cerebrovascular accidents being 7.2 times higher and mortality from acute myocardial infarction (AMI) 9.1 times higher [3, 14]. As young individuals represent the core of the working-age population, their disability and mortality pose a significant socio-medical challenge [6].

One of the primary causes of ischemic heart disease (IHD) is coronary atherosclerosis, which follows a wave-like progression, leading to spontaneous complications such as acute myocardial infarction (AMI) and/or acute coronary syndrome (ACS). In the preclinical stage, there are no symptoms; however, during this period, the vascular wall of the coronary arteries is initially affected. This leads to the formation of lipid spots and the development of atherosclerotic plaques (ASB), accompanied by cascade reactions such as endothelial dysfunction (ED), dyslipidemia (DLP), and an inflammatory process within the plaque [10, 61]. Early clinical signs of ASB manifest as a result of rupture or erosion of the plaque, causing its contents to come into contact with blood elements. This leads to the formation of an atherothrombus. If the coronary artery becomes completely occluded with collateral insufficiency, myocardial tissue necrosis occurs, presenting as AMI. In cases of incomplete occlusion or coronary artery spasm, myocardial ischemia develops, resulting in unstable angina that may present as first-onset, progressive, variant, or early post-infarction angina [72, 75, 78].

The wave-like progression of ASB is characterized by alternating periods of remission, during which the plaque stabilizes with thickening of the fibrous cap and reduction of the lipid core, and periods of exacerbation, during which plaque destabilization occurs. During exacerbations, inflammation intensifies, intraplaque

hemorrhages develop, the fibrous cap thins, and the lipid core enlarges, leading to explosive plaque growth. Clinically, these alternating periods manifest as stable angina and unstable angina [78, 90].

In angina pectoris, the primary complaint of patients is usually a squeezing pain behind the sternum or discomfort in the heart area, radiating to the interscapular area, left shoulder, left arm, back, lower jaw, or epigastric region. These symptoms intensify with physical exertion, emotional stress, or increased blood pressure, and they quickly disappear after rest or the administration of nitroglycerin [127].

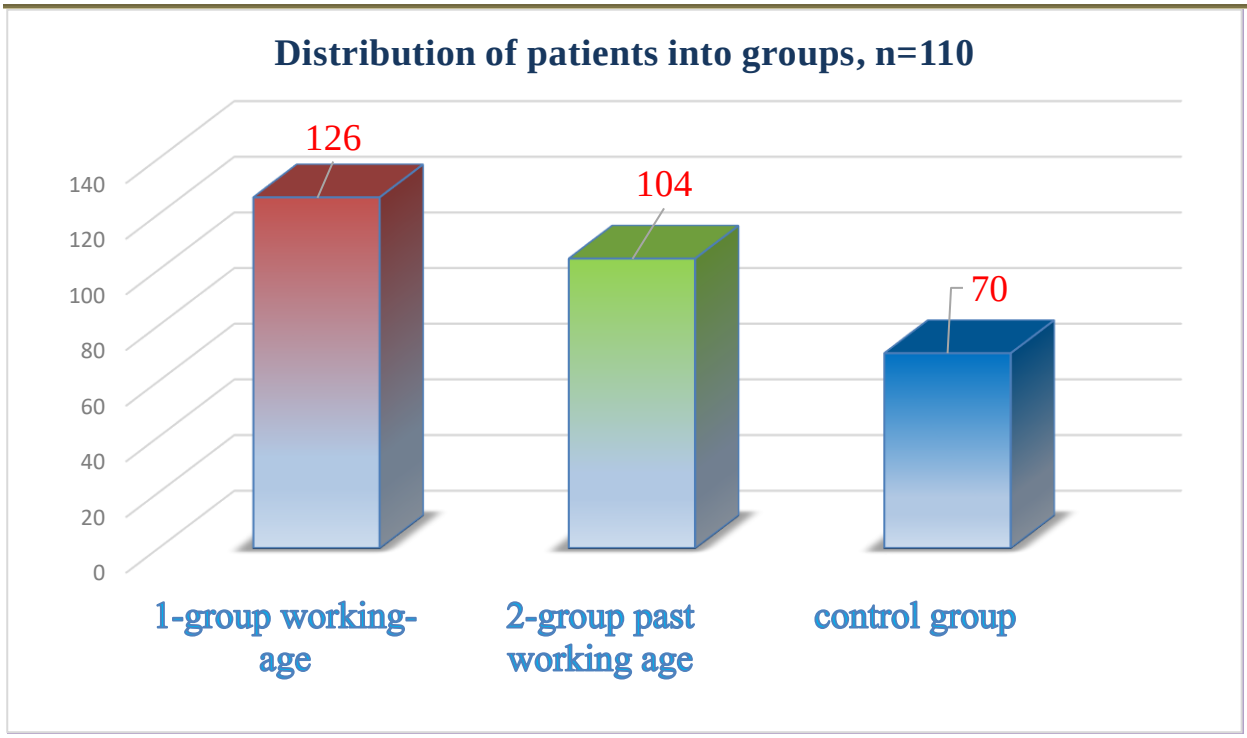
Among patients with IHD, various risk factors (RFs) are often encountered which may either cause or contribute to the development or destabilization of IHD, as some RFs promote an earlier development of various complications. Nowadays, our understanding of the role of RFs in IHD development has been significantly enhanced, leading to substantial changes in the approaches to its diagnosis and treatment [93, 207]. In young individuals, IHD prevention is challenging, as the number of RFs is increasing and affecting an ever-growing portion of the young population, with each young patient having their own set of RFs, making prevention an individual process. In cardiological practice, patients are frequently encountered with two, three, or more RFs simultaneously, many of which are modifiable [151]. In individuals with unstable angina, regardless of the number of RFs present, the prognosis is significantly worse compared to those without them. That is why correcting these RFs in IHD patients should be a fundamental part of their treatment strategy, developed individually for each patient [79].

To enhance the effectiveness of primary prevention in young individuals with IHD, it is necessary to organize comprehensive medical preventive examinations at least twice a year, with attention paid to each individual's lifestyle and RFs, and to develop targeted strategies to address each modifiable RF. Additionally, attention should be given to working conditions and to clarifying the causes of stressful and depressive circumstances, with personalized educational efforts aimed at preventing the development of acute coronary events.

Clinical characteristic of patients

This study is based on observational results from patients with ischemic heart disease (IHD) who were hospitalized between 2021 and 2023 in the departments of somatic resuscitation and emergency therapy Nos. 1 and 2 at the Samarkand Branch of the Republican Scientific Center for Emergency Medical Care (SF RNCEMP), as well as in the IHD departments of the Samarkand Regional Branch of the Republican Specialized Scientific-Practical Medical Center of Cardiology (SRF RSNP MTC).

A total of 230 patients with IHD were examined and divided into two groups based on age. The first main group consisted of 126 (54.8%) patients with IHD of young age, with a mean age of 40.8 ± 15.29 years. The second comparative group included 104 (45.2%) patients with IHD of older-than-young age, with a mean age of 70.9 ± 10.22 years (see Fig. 3.1). The control group consisted of 70 healthy volunteers.



Puc. 3.1. *Distribution of patients into groups depending on age*

The inclusion criteria were as follows: patients aged 18 to 60 years (young age) and patients aged 60 to 74 years (older-than-young age) with a confirmed diagnosis of coronary artery disease (CAD), who provided informed consent to participate.

The exclusion criteria included: patients aged 18 to 85 years for whom the diagnosis of CAD was excluded, patients with severe comorbidities (such as acute cerebrovascular accidents, acute or chronic diseases in the stage of exacerbation), patients with hemodynamically significant heart defects, patients with mental illnesses, and those with a history of traumatic brain injuries.

When distributing patients into groups, the age classification from the WHO (2023) was used, which includes: young age from 18 to 44 years, middle age from 45 to 59 years, elderly age from 60 to 74 years, senile age from 75 to 89 years, and longevity over 90 years.

For determining the severity of unstable angina, a modified classification of Braunwald adopted in 2000 was used, where unstable angina has the following variants: new-onset angina (NOA), progressive effort angina (PEA), variant (Prinzmetal) angina, early post-infarction angina.

All patients underwent clinical and anamnesis evaluations, during which the presence of signs of coronary artery disease (CAD), such as unstable angina variants, resting angina, or previously suffered myocardial infarction, was clarified in men with CAD. Additionally, the presence of risk factors (such as smoking, family history, physical inactivity, stress, hypertension, diabetes, obesity, energy drink consumption, improper nutrition, etc.) and comorbidities contributing to the development or severe course of the disease were assessed.

The assessment of physical status followed standard methodology, with mandatory measurement of blood pressure (BP) and heart rate (HR). BP was measured using the N.S. Korotkov method in a sitting position after a 5-minute rest.

Height and weight were evaluated, and the body mass index (BMI) was calculated using the Broca formula recommended by the WHO committee (1995). BMI was defined as the ratio of body weight in kilograms to height in meters squared:

BMI = weight (kg) / height (m^2)

A normal BMI is considered to be between 20 and 25 kg/m^2. Overweight is defined as a BMI ranging from 25.1 to 30 kg/m^2. First-degree obesity is indicated by a BMI from 30 to 34.99 kg/m^2, second-degree obesity from 35 to 39.9 kg/m^2, and third-degree obesity for a BMI of 40 kg/m^2 or higher.

The goal of our physical examination was to exclude extracardiac causes of pain associated with non-coronary diseases, as well as non-cardiac causes contributing to the exacerbation of myocardial ischemia.

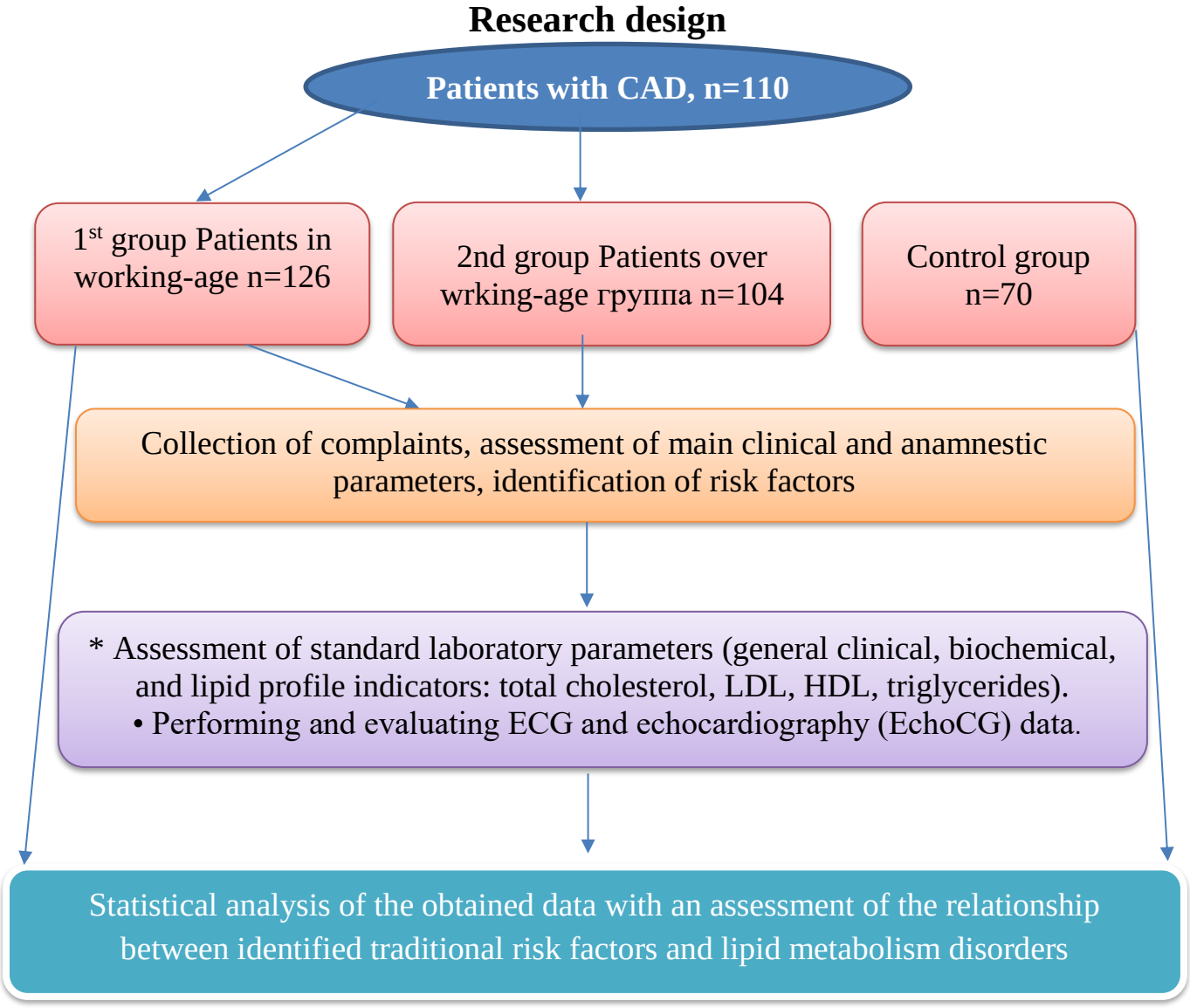


Figure 3.1. *Study design*

Characteristics of patients in the main group and comparison group

During the examination of patients by groups, the following clinical-anamnestic and hemodynamic data were revealed. Almost all examined patients had from 1 to 3 comorbidities. Hypertension (HT) was diagnosed in 15 (27.7%) patients in the first group and was lower than in the second group, where this figure was 12 (26.7%) ($p<0.001$*). Diabetes mellitus (DM) in the medical history was noted in 8 (12.3%) men with coronary artery disease (CAD) and in 10 (22.2%) female patients ($p=0.07$). Overweight/obesity was diagnosed in 14 (36.9%) patients in the first group, which was significantly lower than in the second group, where it was noted in 18 (71.1%) patients ($p<0.001$*).

Anemia was observed in the first group in 27 (41.5%) patients, and in the second group in 36 (57.8%) ($p=0.24$). In 3 (4.6%) patients in the first group and in 1 (2.22%) patient in the second group ($p=0.01$*), a history of previously suffered acute cerebrovascular accidents was noted. Chronic ischemic heart disease (CIHD) was observed in the first group in 15 (23.1%) patients, and in the second group in 9 (20%) patients ($p=0.004$*). Chronic obstructive bronchitis (COPD) in the medical history was found in 5 (7.7%) patients in the first group and in 2 (4.44%) patients in the second group ($p=0.31$

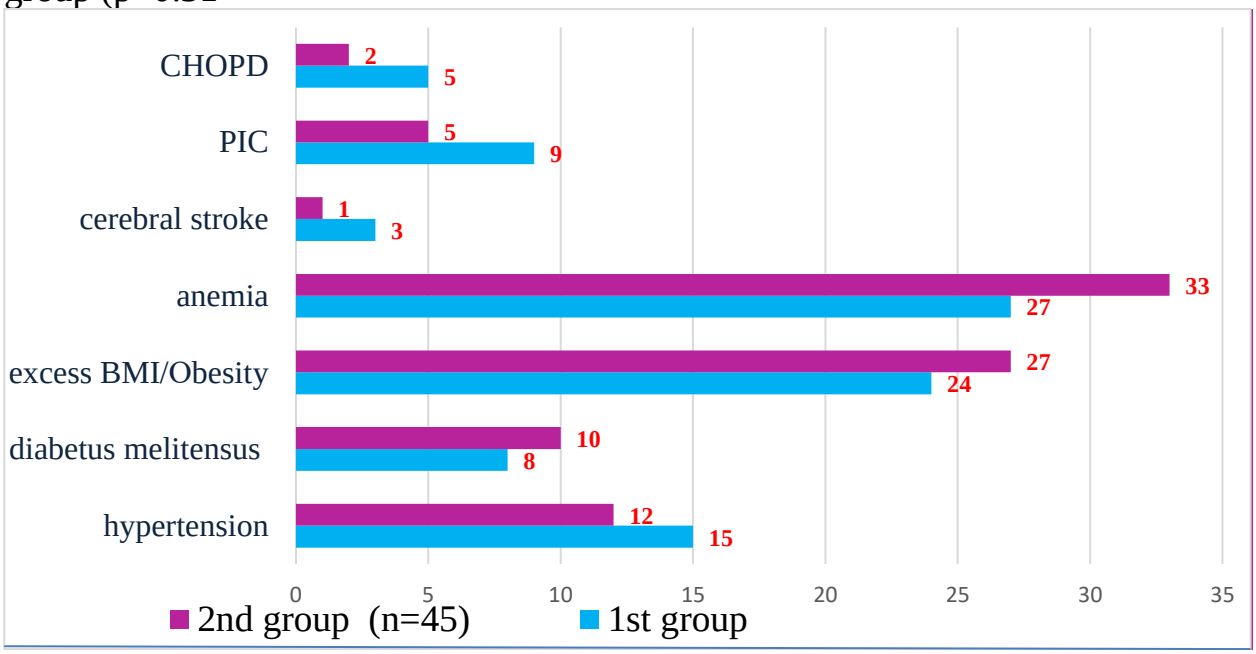


Fig. 3.2. *Frequency of accurrence of concomitant pathologies in the study group*

All patients received medication therapy on the day of admission: β-blockers, nitrates, anticoagulants, antiplatelet agents (ASA/clopidogrel), statins, ACE inhibitors; this treatment was continued dynamically. In addition, a comparative analysis was conducted on the effect of the cardioprotector Tivorel in combination with traditional therapy on the clinical course of CAD.

Clinical-anamnestic and physical examinations were carried out to exclude extracardiac causes of pain in the pericardial area, non-coronary heart diseases, as well as extracardiac causes provoking myocardial ischemia (hypotension, hyperthermia,

anemia, etc.), and to identify cardiac causes that exacerbate or contribute to myocardial ischemia.

Clinical characteristics of individuals in the control group

Eighty-six practically healthy volunteers aged 22 to 44 years entered the control group, with an average age of 37.6±5.3 years. The inclusion criteria for individuals in the control group were the absence of chronic cardiovascular diseases (CVD), normal blood pressure levels, and clinical data from exercise testing indicating no CAD.

The average BMI was 24.6±3.08 kg/m². Normal body weight was found in 42 (38.2%) individuals, 32 (29.1%) individuals had overweight, and obesity of the first degree was only observed in 12 (10.9%) individuals. Early-stage CVD was present in 33 (30%) men in the control group. There were 38 (34.5%) smokers, and the average smoking index was 0.33. Stressful conditions were noted in 30 (27.3%) individuals. Alcohol consumption was reported in 24 (21.8%) (Table 2.2). The consumption of energy drinks was noted in 11 (10%).

Table 2.2

General characteristics of the control group

Name of indicators	**Control group (n=110)**
BMI, kg/м^2	24,6±3,08
Normal body weigh	42 (38,2%)
overweigh, kg/м^2	32 (29,1%)
1st degree obesity	12 (10,9%)
Burdened heredity	33 (30%)
Smoking	38 (34,5%)
Smoking index	0,33
Stress	30 (27,3%)
Alcohol consumption	24(21,8%)
Consupmtion of energy drinks	11 (10%)

The clinical-anamnestic characteristics and the frequency of risk factors in patients with CAD and the control group

This study is based on data from 110 patients diagnosed with coronary artery disease (CAD), who were treated and admitted to the emergency and cardiology departments No. 2 of the Samarkand branch of the Republican Scientific Center for Emergency Medical Assistance (SFC REMA), as well as the CAD department at the Samarkand Regional Branch of the Republican Specialized Scientific-Practical Medical Center for Cardiology (SRSSPMC). The patients' ages ranged from 22 to 44 years. They were divided into two groups based on gender: the first group consisted of 65 (59%) male patients, with an average age of 39.6 ± 5.1 years, while the second group had 45 (41%) female patients, with an average age of 38.5 ± 4.6 years. The control group comprised 86 healthy individuals.

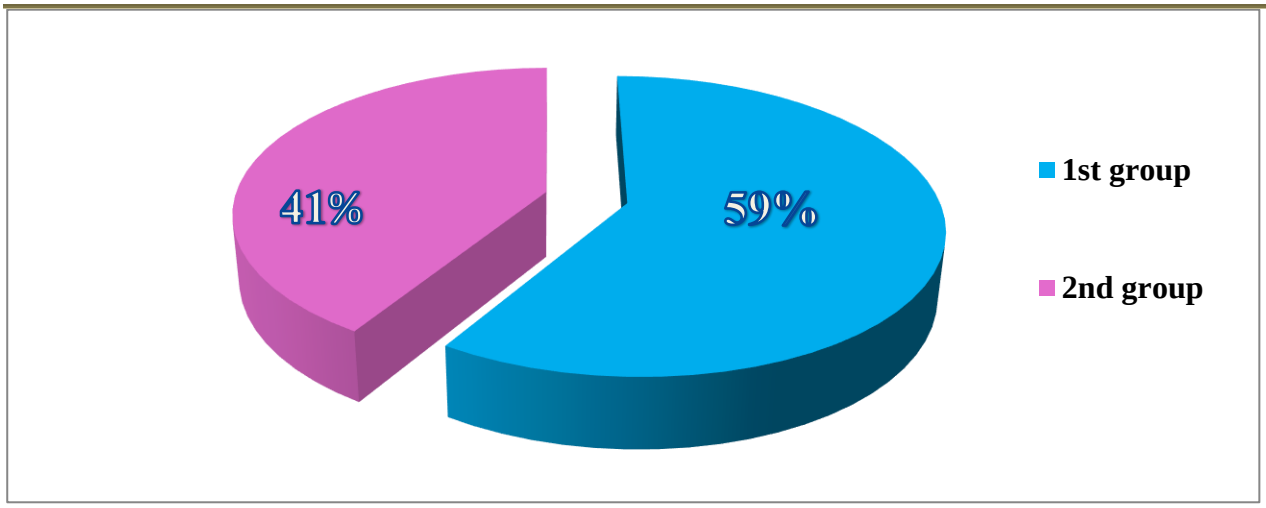


Fig. 3.1.1. Distribution of patients into groups depending on age.

All patients were evaluated based on their clinical history, along with standard clinical and biochemical tests, which included measurements of lipid metabolism. Physical assessments were conducted using established methods, including mandatory measurements of the patient's weight and height, as well as blood pressure (BP) and heart rate (HR). The body mass index (BMI) was calculated using the Broca formula, as recommended by the WHO committee (1995). BMI was calculated by dividing weight in kilograms by the square of height in meters. A BMI between 20 and 25 was considered normal, while a BMI ranging from 25.1 to 30 indicated overweight, and a BMI over 30 signified obesity. Blood pressure was measured using the Korotkov method with the patient seated, following at least a 5-minute rest period.

During the history taking for patients with CAD, the presence of CAD (previous myocardial infarction, stable or unstable angina) and risk factors (atherosclerosis in other vascular areas, hypertension, smoking, diabetes, obesity, alcohol consumption, energy drinks, poor diet) were assessed. The history also focused on the period preceding the development of acute coronary syndrome (ACS) and factors that provoked the onset of the current disease (excessive physical exertion, psychological stress, physical inactivity, unhealthy lifestyle), as well as information about early manifestations of cardiovascular diseases in close relatives.

Patients were divided into groups based on the clinical course of CAD. According to ECG results and clinical manifestations, first-time angina (FTA) was recorded in 23 (35.4%) patients in the first group, while in the second group, FTA was noted in 19 (42.2%) patients ($p<0.001$). Progressing stable angina (PSA) was identified in 35 (53.8%) patients in the first group and in 20 (18.2%) patients in the second group ($p=0.02$). Q-wave myocardial infarction (Q-MI) was observed in 7 (10.8%) patients in the first group and in 6 (13.3%) patients in the second group ($p=0.09$).

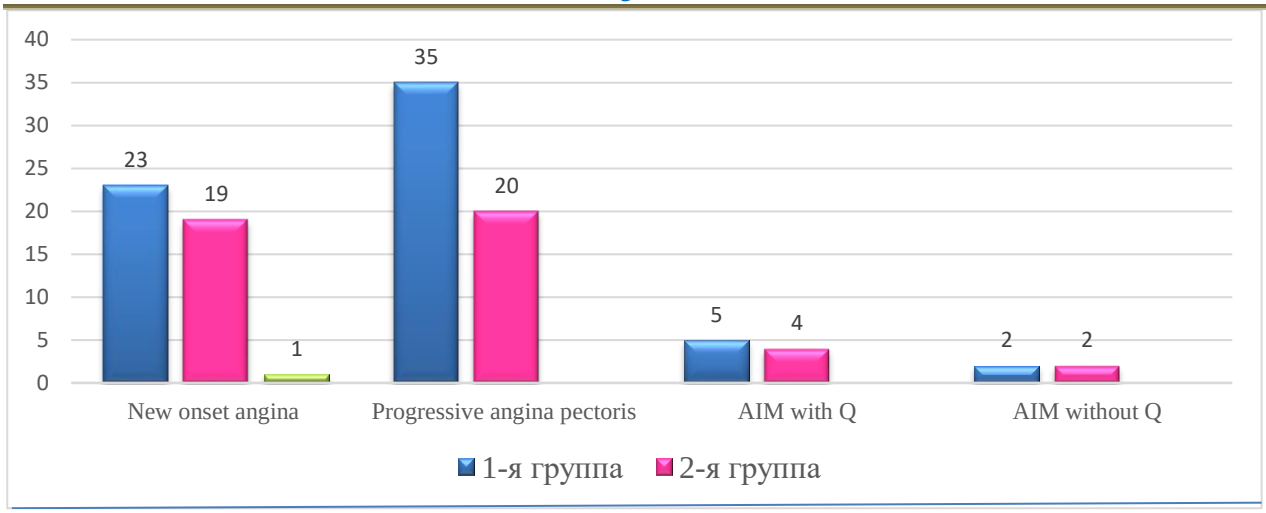


Fig. 3.1.2. Distribution of patients depending on the clinical course of CHD

When interviewing all patients with coronary artery disease (CAD), special attention was paid to the main complaint of chest pain behind the sternum. Based on the frequency of angina attacks during the day, the following data were obtained. Angina attacks occurring 3–5 times per day were observed in Group 1 in 27 (13.5%) patients and in Group 2 in 14 (6.7%) patients ($p<0.0001$). Angina attacks occurring 6–8 times per day were noted in 25 (67.5%) patients in Group 1 and in 22 (78.8%) patients in Group 2 ($p=0.001$). Attacks occurring more than 9 times per day were reported in 12 (19%) patients in Group 1 and in 9 (14.4%) patients in Group 2 ($p>0.05$) (Fig. 3.1.3).

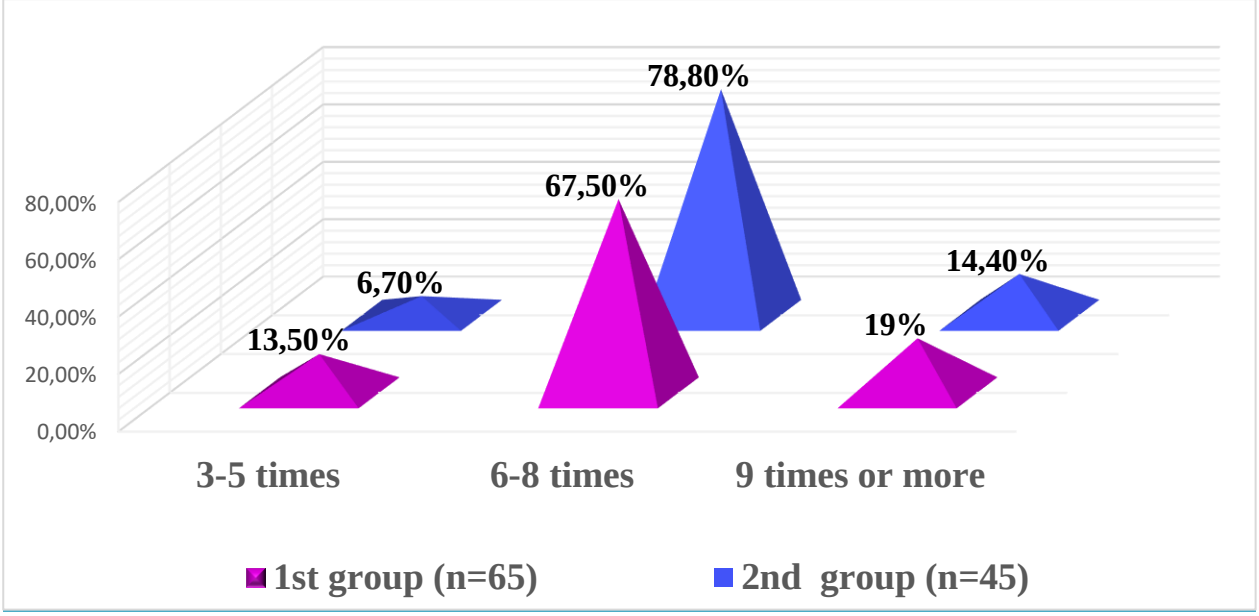


Fig.3.1.3 Distribution of patients by frequency of occurenceof angina attacks during the day

When interviewing all patients with coronary artery disease (CAD), attention was paid to the time of onset of chest pain during the day. Based on the time of occurrence of angina attacks throughout the day, the following data were obtained. Angina attacks occurring between 01:00 and 06:00 were noted in Group 1 in 7 (13.5%) patients and in Group 2 in 4 (6.7%) patients ($p<0.0001$). Angina attacks occurring between 06:00 and 12:00 were observed in 18 (67.5%) patients in Group 1 and in 13 (78.8%) patients in

Group 2 (p=0.001). The occurrence of attacks between 12:00 and 18:00 was noted in 24 (19%) patients in Group 1 and in 16 (14.4%) patients in Group 2 (p>0.05). Angina attacks occurring between 18:00 and 24:00 were recorded in 16 (13.5%) patients in Group 1 and in 12 (6.7%) patients in Group 2 (p<0.0001) (Fig. 3.1.4).

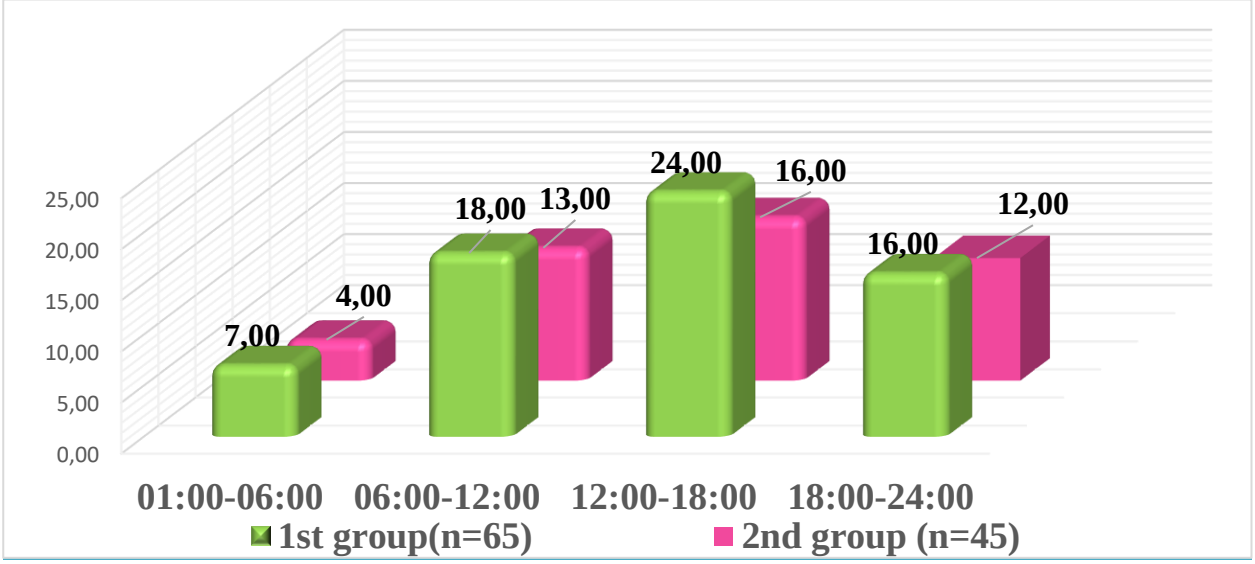


Fig. 3.1.4 Distribution of patients by the time of occurrence of angina attacs during the day

When studying the intensity of anginal pain using the 10-point Wong-Baker FACES Pain Rating Scale, the following data were obtained. In patients with congenital heart disease (CHD), the pain syndrome ranged from 1 to 3 points and was observed only in 30 (23.8%) patients in Group 1. In patients with chronic heart failure (CHF), the pain syndrome ranged from 4 to 6 points and was recorded in 51 (40.5%) patients in Group 1 and in 58 (55.8%) patients in Group 2 (p<0.05). In patients with acute coronary syndrome (ACS), the pain intensity ranged from 7 to 9 points and was noted in 38 (30.2%) patients in Group 1 and in 36 (34.6%) patients in Group 2 (p=0.34). Pain with an intensity of 10 points was observed in patients with acute myocardial infarction (AMI) and was recorded in 7 (5.5%) patients in Group 1 and in 10 (9.6%) patients in Group 2 (p=0.11) (Fig. 3.9).

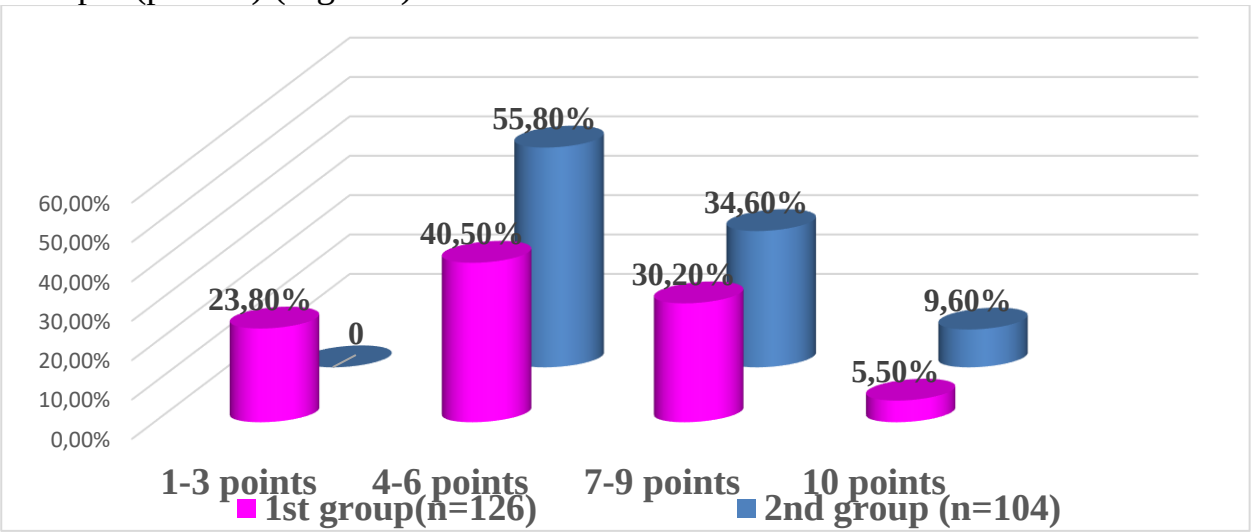


Рис. 3.9. Distribution of patients by pain intensity in points on the 10-point Wong-Biker scale

During the investigation of pain syndrome in young and middle-aged patients based on their history of COVID-19 infection, the following findings were recorded: Among patients with a history of COVID-19, the pain syndrome was described as compressive and was observed in 22% of cases. In contrast, patients experiencing acute myocardial infarction (AMI) without prior COVID-19 infection reported a stabbing type of pain, which was noted in 18% of cases.

Depending on the prevalence of risk factors (RF), the following indicators were identified. One of the main RFs—smoking—was found in 37 (56.9%) patients in Group 1 and in 9 (20%) patients in Group 2 ($p<0.001$). Arterial hypertension (AH) was observed in 18 (27.8%) patients in Group 1 and in 12 (26.7%) patients in Group 2 ($p<0.001$). Diabetes mellitus (DM) was identified in 5 (7.7%) patients in Group 1 and in 2 (4.44%) patients in Group 2 ($p<0.001$). Overweight/obesity was noted in 14 (21.5%) patients in Group 1 and in 18 (26.7%) patients in Group 2 ($p<0.001$). A positive family history was present in 16 (40%) patients in Group 1 and in 15 (55.6%) patients in Group 2 ($p<0.01$). Chronic stress was identified in 26 (40%) patients in Group 1 and in 24 (53.3%) patients in Group 2 ($p<0.001$). Alcohol consumption was reported in 32 (49.2%) patients in Group 1 and in 5 (11.1%) patients in Group 2 ($p=0.05$) (Fig. 3.1.5).

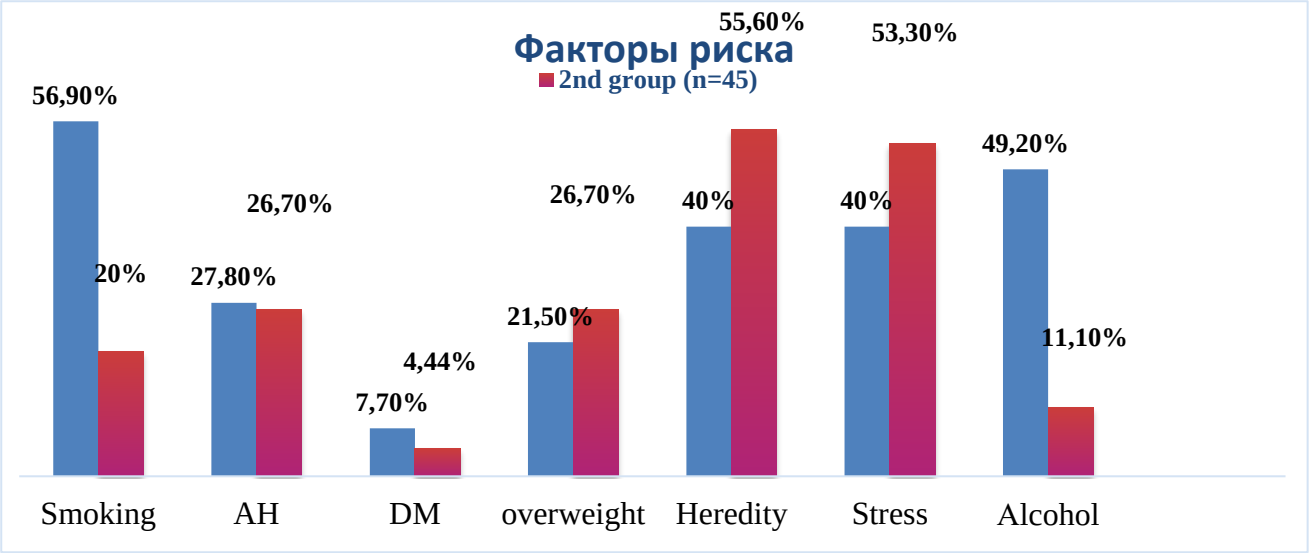


Fig. *3.1.5. Distribution of patients depending on the prevalence of risk factors*.

According to anthropometric data, the following changes were identified. In Group 1, the average height of patients was 1.77 m, while in Group 2 it was 1.64 m ($p=0.0001$). The average weight in Group 1 was 76.7 kg, and in Group 2 it was 83.2 kg ($p=0.05$). The BMI in Group 1 was 24.6 kg/m², while in Group 2 it was 27.7 kg/m² ($p=0.01$). Among patients in Group 1, normal body weight was identified in 32 (49.2%) patients, while in Group 2 it was observed in only 18 (40%) patients ($p<0.001$). Overweight was found in 13 (35.4%) patients in Group 1 and in 15 (42.2%) in Group 2 ($p<0.001$). Obesity Class I was recorded in 1 (15.4%) patient in Group 1 and in 3 (15.6%) patients in Group 2 ($p<0.001$) (Table 3.1).

Table 3.1

Characteristics of patients baserd on anthropometric data.

Anthropometric indicators	1st group (n=65)	2nd group (n=45)	Mann-WhitneyWilcoxon .
Heigh (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 body weight Нормальное масса тело	32 (49,2%)	18 (40%)	<0,001
Overweight	23 (35,4%)	19 (42.2%)	<0,001
Obesity of the 1st degree	10 (15,4%)	7 (15,6%)	<0,001

Conclusion to the Chapter

Thus, the analysis of data from the indicated groups based on risk factors showed that male patients with coronary artery disease (CAD), in most cases, have the same risk factors as female patients with CAD, which allows them to be considered potential candidates for a more severe course of the disease in the future. Among young individuals, common risk factors include smoking, stress, overweight/obesity, arterial hypertension, and alcohol consumption — all of which are modifiable. The ability to predict the risk of developing cardiovascular disease in young people based on these risk factors opens new perspectives for forming a strategic approach to managing young individuals at high risk of adverse outcomes.

Comparison of laboratory and Instrumental Indicators in CAD Patioents by Age

Laboratory Data

To identify significant predictors of poor prognosis in coronary artery disease (CAD), key parameters from general and biochemical blood tests were analyzed for all patients included in the study (n=110). These parameters are essential during the inpatient treatment of CAD patients.

Recent studies continue to refine the prognostic value of inflammatory markers in CAD patients [164, 173]. However, the complete blood count (CBC) remains a simple, accessible, and routinely conducted test that serves as the starting point in diagnostic evaluation. It is well established that leukocytes play a pivotal role in plaque destabilization within the coronary arteries at the onset of CAD. Current evidence suggests that elevated leukocyte levels in CAD patients act as an independent prognostic marker for adverse outcomes in both the early and late stages of the disease [144].

Some studies suggest that the monocyte count, measured at the time of hospital admission in CAD patients, may also carry independent prognostic value and is used for risk stratification in this patient group. In our study, a comparative analysis of the leukocyte formula between gender groups revealed statistically significant differences in both the percentage and absolute count of monocytes (8.0 vs. 7.0, p=0.025, and 0.90 vs. 0.70, p=0.022, respectively) (Table 3.2.1).

Table 3.2.1

Comparative characteristics of the indicators of thye general blood test parametres in patients with coronary heart disease of the general group and depending on gender

Parameter	Total sample (n=110)	Men up to 45 (n=65) (2)	Women 45 years old (n=45) (3)	*p2-3*
Hemoglobin (r/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
Eosinophilis, %	1,0 (0,0–2,0)	0,0 (0,0–2,0)	1,0 (0,0–1,5)	0,943
Rod nuclear neutrophilis, %	1,0 (1,0–3,0)	1,5 (1,0–3,0)	1,0 (1,0–2,0)	0,620
Segmented nuclear neutrophilis., %	67 (60,0–74,0)	66 (58–73)	68,5 (60–74)	0,238
Total quantity of neutrophilis %	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

In the study of general biochemical blood analysis indicators, it was noted that female patients had a glomerular filtration rate (GFR) that was 6.8 ml/min lower compared to male patients, with values of 92.7 ± 10.5 ml/min and 99.5 ± 9.5 ml/min, respectively ($p < 0.0001$). In the control group, the average GFR was 109.8 ± 18.5 ml/min ($p = 0.26$).

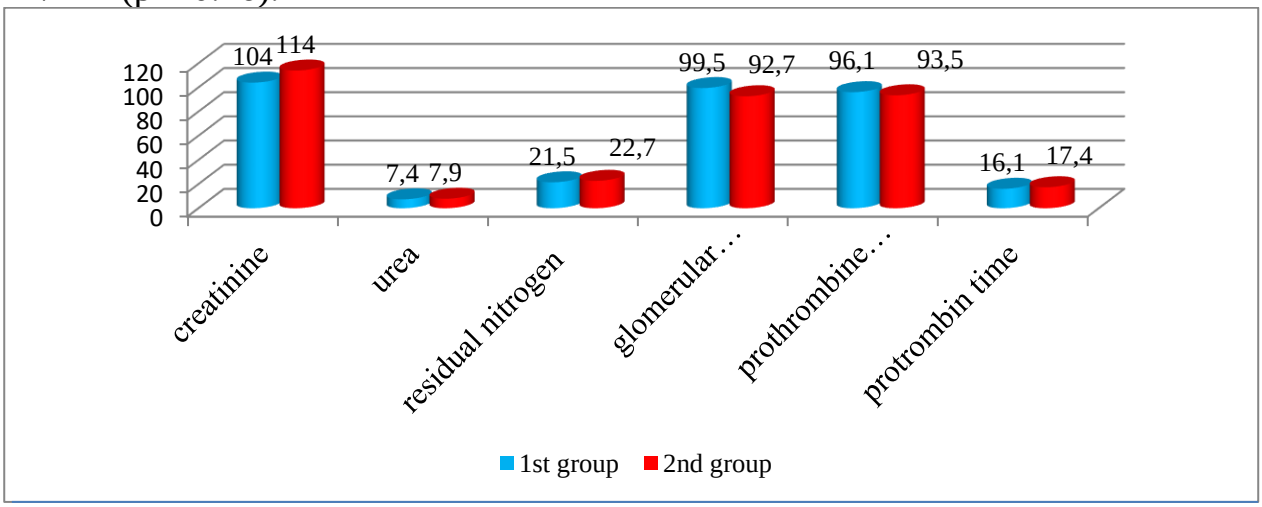


Fig. 3.2.1. Indicators of biochemical blood analysis in patients with CAD

Patients with ACS without ST-segment elevation and with signs of anxiety and depression had significantly high levels of a number of hormones, which are presented in the table.

The adrenaline levels were 118.4 ± 23.6 pg/ml, which indicated not only signs of anxiety but also an acute period of destabilization of CAD. These values among patients with ACS without NVN also reached the upper limit of normal and were 111.8 ± 22.3 pg/ml. The cortisol levels among patients with ACS+NVN were 332.4 ± 66.4 mmol/l, which were also significantly higher compared to patients with SA, whose level was 245.7 ± 49.1 mmol/l. It should be noted that the thyroid hormones had significantly high levels in the main group as opposed to patients with isolated ACS and patients with SA.

Thus, the research we conducted showed that signs of the psycho-emotional state manifest themselves not only in terms of clinical analysis, but also in terms of laboratory analysis.

The rate of some hormones in people wit CHD

I				
Adrenaline, pg/мл	118,4±23,6	111,8±22,3	93,4±18,6	0,001
Noradrinaline , pg/мл	252,7±50,5	278,3±55,6	450,5±90,1	0,001
Cortisol, mmol/l	332,4±66,4	287,7±57,5	245,7±49,1	0,001
TSH, mmU/l	5,4±1,08	3,7±0,74	2,8±0,56	0,001
T3 gen, nmol/l	2,7±0,54	1,6±0,32	1,7±0,34	0,001
T3 free, nmol/l	6,2±1,24	3,4±0,68	3,8±0,78	0,001
T4 gen, nmol/l	139,7±27,9	97,4±19,48	83,2±16,64	0,001
T4 free, nmol/л	25,6±5,12	16,3±3,26	10,9±2,18	0,001

During the analysis of the blood lipid profile, elevated levels of total cholesterol (TC), low-density lipoprotein (LDL), and triglycerides (TG) were observed in both groups. The TC level in the second group was 0.26 mmol/L higher than in the first group, with values of 7.14 mmol/L and 6.88 mmol/L, respectively ($p = 0.049$*). In contrast, LDL levels in the first group were 0.37 mmol/L higher, with values of 4.50 mmol/L compared to 4.13 mmol/L in the second group ($p < 0.001$*), indicating lipid metabolism disturbances in CAD patients.

Regarding high-density lipoprotein (HDL), no statistically significant differences were found between the groups: 1.0 mmol/L in the first group and 0.96 mmol/L in the second group ($p = 0.03$), although HDL levels were below normal in the elderly group. In terms of triglycerides, the first group had significantly higher levels (3.62 mmol/L), compared to 3.19 mmol/L in the second group ($p < 0.001$*).

The atherogenic coefficient (AC) was elevated in both groups, with values of 5.88 in the first group and 6.42 in the second group, while the normal range should not exceed 3.0 (p = 0.03) (Figure 6).

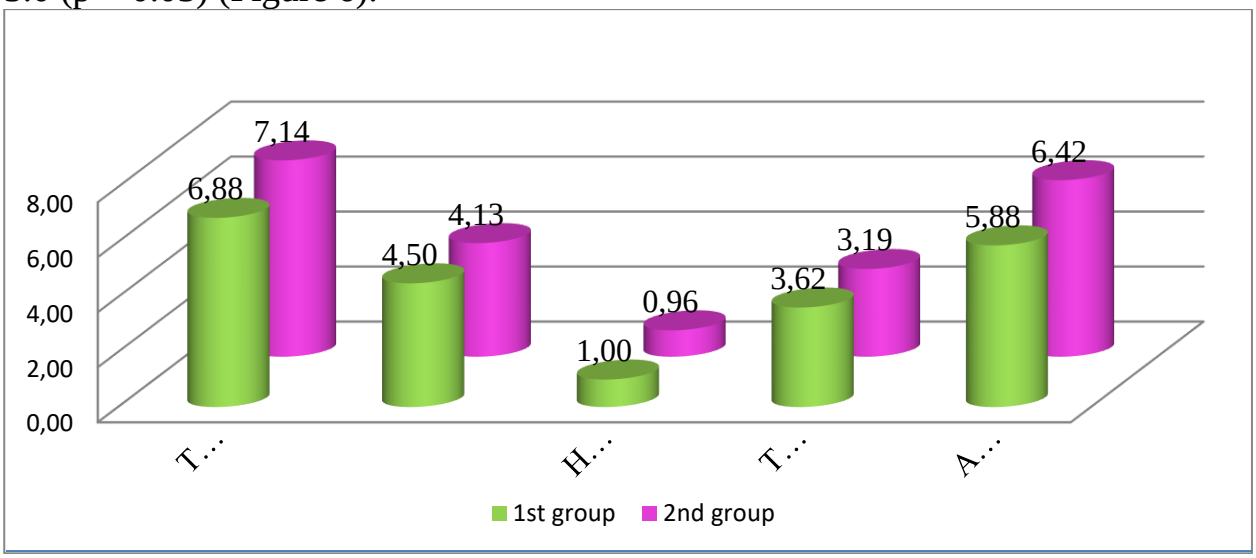


Fig. 3.2.2. Indicators of lipid metabolism in patients with NBS by groups.

In addition, younger patients had comorbidities that could also exacerbate the course of the disease. Many younger patients were noted to have excess body weight, which was revealed during the study of the lipid spectrum of blood. Early detection of RF, combating excess weight, and timely treatment of comorbidities and lipid metabolism disorders in young men contribute to reducing the development of CVD.

Electrocardiographic data.

Upon admission, all patients underwent ECG studies on the Fukuda device, where pathological criteria were identified such as ST segment elevation or depression, T wave changes, the presence of pathological Q waves, regression of the R wave in V1-V4 leads, rhythm disturbances, and the appearance of new complete left bundle branch block, which also indicated instability of angina.

Regarding the localization of ischemic changes on the ECG, the following data were revealed. Ischemic changes in the anterior wall were noted in group 1 in 27 (41.5%) patients, and in group 2 in 15 (33.3%) patients (p=0.99). Ischemia of the posterior wall of the left ventricle (LV) was observed in 26 (40%) patients in group 1, while in group 2 it was found in 17 (37.8%) patients (p=0.45). Ischemic changes in the anteroseptal wall were twice as high in group 2, noted in 7 (15.6%) patients, while in group 1 it was 7 (10.8%) patients, respectively (p=0.14). Ischemia of the lateral wall was identified in group 1 in 5 (7.8%) patients, and in group 2 in 6 (13.3%) patients (p=0.81). Ischemia of two or more walls was observed in group 1 in 28 (43.1%) patients, and in group 2 in 19 (42.2%) patients (p=0.79) (Fig. 3.3.1

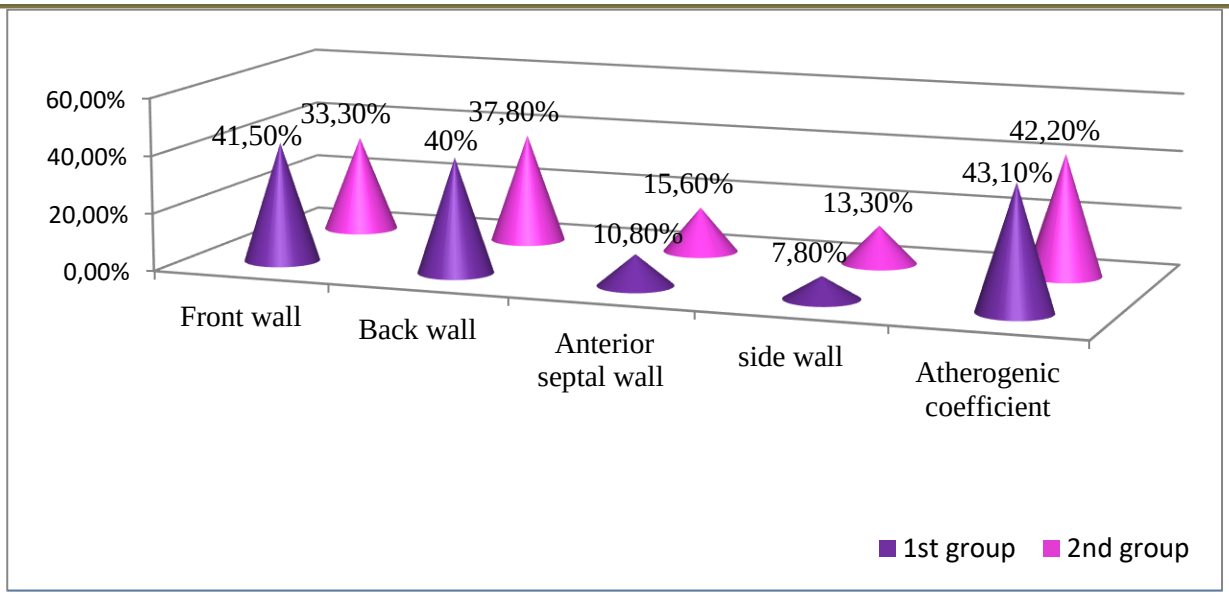


Figure 3.3.1 Distribution in patients with CAD depending on ischemic damage to the left ventricle myocardium.

According to ECG data, in young men with CAD compared to female patients, the indicators of damage to the anterior and posterior walls were high, at 41.5% and 40% versus 33.3% and 37.8%, respectively. T-wave inversion was noted in group 1 in 81 (64.3%) cases, while in group 2 it was observed in 58 (55.8%) patients ($p<0.05$*). ST segment elevation was observed in 26 (20.6%) patients in group 1 and 27 (25.9%) in group 2 ($p=0.35$). ST segment depression was noted in group 1 in 12 (9.5%) patients and in group 2 in 9 (8.7%) patients ($p=0.82$). Q-wave myocardial infarction (MI) was identified twice as often in group 2, with 10 (9.6%) patients compared to 5 (3.7%) in group 1 ($p=0.09$). Non-Q-wave MI was found only in group 1, totaling 2 cases (1.6%). Scarring changes were noted in 15 (11.9%) patients in group 1 and in 31 (29.8%) patients in group 2 ($p<0.001$*). WPW syndrome was identified only in group 1 in 3 (2.38%) patients (p=NA). Heart rhythm disturbances in the form of atrial fibrillation were recorded in 3 (2.38%) young patients and in 5 (4.8%) elderly patients ($p>0.05$). Ventricular extrasystole was noted in 3 (2.38%) patients in group 1 and in 1 (0.96%) patient in group 2 ($p>0.05$). The frequency of blockages in both groups was the same, totaling 6 (4.76%) and 6 (5.78%), respectively ($p>0.05$) (Table 3.10).

Table 3.10.

ECG date in patients with coronary heart disease and the contro group

Indicators	1st group (n=126)	2nd group (n=104)	Mann-Whitney-Wilcoxon tests
T-wave inversion	81 (64,3%)	58 (55,8%)	1vs2:p=0,01*
ST segment elevation	26 (20,6%)	27 (25,9%)	1vs2: p>0,05
ST segment depression	12 (9,5%)	9 (8,7%)	1vs2: p>0,05
AIM with Q-wave	5 (3,7%)	10 (9,6%)	1vs2: p=0,09
AIM without Q-wave	2 (1,6%)	-	1vs2: NA
Cicatrical changes	15 (11,9%)	31 (29,8%)	1vs2: 0,01*
WPW syndrome	3 (2,38%)	-	1vs2: NA

Atrial fibrillation	3 (2,38%)	5 (4,8%)	1vs2: p>0,05
Ventricular extrasystole	3 (2,38%)	1 (0,96%)	1vs2: p>0,05
Blockades	6 (4,76%)	6 (5,78%)	1vs2: p>0,05

Echocardiographic data.

According to the results of the EchoCG, the following changes were identified in the studied groups. The left ventricular ejection fraction (LVEF) in group 1 averaged 53.6%, while in group 2 it was reduced to 50%±8.4 ($p<0.01$). In the control group, the LVEF averaged 56%±9.0 ($p=0.48$). The end-diastolic volume (EDV) in group 1 averaged 140.3±40.0 ml and in group 2 it was 152±49.03 ml ($p=0.09$), while in the control group it was 120±20.2 ml ($p<0.05$). The end-systolic volume (ESV) was 78.7±25.2 ml in group 1 and 84.6±36.2 ml in group 2 ($p=0.11$), while in the control group it was 56±14.4 ml ($p<0.001$*).

One area of hypokinesis was identified in group 1 in 30 (46.2%) patients and in group 2 in 22 (48.9%) patients ($p=0.78$). Hypokinesis of more than two zones was noted in group 1 in 35 (53.8%) patients and in group 2 in 23 (51.1%) patients ($p=0.01$*). Akinesis was identified in group 1 in 24 (36.9%) patients and in group 2 in 15 (45.5%) patients ($p=0.01$*). In the control group, no areas of hypo- or akinesis were found according to EchoCG data (Table 3.3.1).

Table 3.3.1

EchoCG indicators in patients with CAD at a young age depending on gender and the control group.

Indicators of EchoCG	1st group	2nd group	Control group
Ejection fraction (%)	53,6%±8,2	50%±8,4	56%±9
End diastolic volume (ml)	140,3±40	152±49,03	120±20,2
End systolic volume (ml)	78,7±25,2	84,6±36,2	56±14,4
1hypokinesis zone	30 (46,2%)	22 (48,9%)	0(0%)
2 hypokinesis zone	35 (53,8%)	23 (51,1%)	0 (0%)
Akinesis zone	24 (36,9%)	15 (45,5%)	0 (0%)

Thus, according to the ECG data, ischemic damage of more than two walls was most often observed in young men than in women. The average LVEF in group 1 was 53.6%, while in group 2 it was reduced by 3.6% and amounted to 50%. Hypokinesis of more than two zones was noted in group 1 at 2.7% more than in patients in group 2, amounting to 53.8% and 51.1%, respectively.The area of akinesis was identified in

group 1 in 24 (36.9%) patients, while in patients in group 2, areas of akinesis were found 9% more often, amounting to 15 (45.5%). The identification of these data indicates a severe course of the disease, especially at a young age, and requires timely and rational treatment, as this can lead to early disability and fatal outcomes.

Indicators of Cardiac-Specific Markers of Myocardial Necrosis in Patients with Acute Coronary Syndrome and Acute Myocardial Infarction

Using a qualitative rapid test for Troponin T (Trop T) from Roche, cardiac troponin T was determined, and an increase in its concentration above 0.1 ng/ml with the appearance of two stripes was considered a positive test. Cardiac troponin I and the metabolic protein creatine phosphokinase (CK-MB) were determined using the immunoassay analyzer Triage® MeterPro (BIOSITE, USA).

In patients with ACS and AMI, the following indicators were identified in blood tests for cardiac-specific biomarkers. Creatine phosphokinase (CK) in patients in group 1 averaged 195±67.4 U/L, while in group 2 it was 202±48.0 U/L ($p>0.05$). CK-MB in group 1 was 26.1±7.66 U/L, and in group 2 it was 26.6±4.79 U/L ($p>0.05$). Troponin I in group 1 averaged 0.135±0.095 ng/ml, while in group 2 it was 0.316±0.289 ng/ml ($p<0.05$). Troponin T averaged 0.012±0.098 ng/ml in group 1 and 0.028±0.028 ng/ml in group 2 ($p>0.05$) (Table 3.12).

Table 3.12

Indicators of cardiospecific markers of myocardial necrosis in patients with acute coronary syndrome and AMI in the study group

Indicators of cardiovascular markers of myocardial necrosis	1st group	2nd group	Mann-Whitney-Wilcoxon test
Creatine phosphokinase (26-192 U/L)	195±67,4	202 ±48,0	p>0,05
MV- creatine phosphokinase (до 24 U/L)	26,1±7,66	26,6±4,79	p>0,05
Troponin I (0,16 нг/мл)	0,135±0,095	0,316±0,289	p<0,05
TroponinT (0,010 нг/мл)	0,012±0,098	0,028±0,028	p>0,05

Conclusion of the Chapter

The results of the study revealed that patients with VBS and PSN had lower scores compared to those with AMI in both young and elderly age groups. Anginal attacks occurring 6 to 8 times a day were most frequently observed in 85 (67.5%) patients in group 1 and 82 (78.8%) patients in group 2, indicating the severity of the disease in both groups.

ECG findings showed that ischemic damage to more than two walls was more commonly observed in younger individuals, while in elderly men, scar changes were more prevalent, likely due to a history of previous AMI. The average left ventricular ejection fraction (LVEF) in group 1 was 54.6%, while in group 2, it decreased by 3.6%, reaching 51%. Hypokinesis in more than two zones was noted in group 1 at a rate 2.1% higher than in the elderly patients, with 44.4% and 42.3%, respectively.

Akinesis was detected in group 1 in 32 (25.4%) patients, while in elderly patients, akinetic areas were found 15% more often, totaling 42 (40.4%). The identification of these data indicates a severe course of the disease, especially at a young age, and requires timely and rational treatment, as this may lead to early disability and fatal outcomes.

CHAPTER 3.
The role of Dyslipidemia in the destabilization of CAD in working-age individuals

Currently, the role of dyslipidemia (DLP) as a risk factor in the development and progression of cardiovascular diseases, particularly coronary artery disease (CAD) caused by atherosclerotic changes, is widely recognized. Disruptions in lipid metabolism and lipoprotein levels are influenced by a range of factors, including the patient's age and gender, as well as external factors such as dietary habits, food composition, meal frequency, physical inactivity, and an unbalanced diet. Additionally, internal conditions like hormonal fluctuations and digestive system dysfunctions also play a significant role. In DLP, lipid metabolism is disturbed through several pathways, leading to either an increase or decrease in their levels in the blood or a change in the performance of their functions. These disturbances can be independent, may be caused by other diseases, or may be combined with other RFs that contribute to the development of atherosclerosis. In DLP, there is a wide spectrum of disturbances in lipid metabolism, among which special attention is paid to TC, LDL-C, and TG, as according to many randomized studies, it has been noted that a reduction in the levels of TC and LDL-C leads to a decrease in morbidity and mortality from CVD. In DLP, an atherogenic lipid triad is observed, including a moderate increase in the level of TG, a decrease in the level of HDL-C, and an increase in the number of small LDL particles, and these lipids are important indicators in the prevention and treatment of patients with CVD, since a reduction in LDL-C by every 1.0 mmol/L (40 mg/dL) reduces the morbidity and mortality from CHD by 22%. With an increase in LDL-C, regression of the ASP occurs.

According to many scientific studies, there is a direct correlation between body weight and overall mortality, and with a BMI of more than 35 kg/m², mortality is the highest. In the development of CVD, the type of obesity is very significant, and in the case of abdominal obesity, white fat accumulates in the mesentery and omentum, which is an unfavorable predictor of the development of ACE. In men of any age, the abdominal type of obesity is most common regardless of body weight, and this is one of the modifiable RFs for the incidence of CAD in men. One of the most important problems in recent times is reducing LDL-C levels for patients with CVD in various categories, and lowering LDL-C to 1.4 mmol/L is considered the optimal option. Currently, the role of dyslipidemia (DLP) as a risk factor in the development and progression of cardiovascular diseases, particularly coronary artery disease (CAD) caused by atherosclerotic changes, is widely recognized. Disruptions in lipid metabolism and lipoprotein levels are influenced by a range of factors, including the patient's age and gender, as well as external factors such as dietary habits, food composition, meal frequency, physical inactivity, and an unbalanced diet. Additionally, internal conditions like hormonal fluctuations and digestive system dysfunctions also play a significant role.

The process of atherosclerosis consists of several stages: damage to the vascular wall and activation of endothelial cells with the production of immunocompetent cells; transformation of macrophages and monocytes into foam cells with phagocytosis of oxidized LDL; formation of a fibrous cap of the ASP upon the death of foam cells; migration and proliferation of vascular smooth muscle cells; rupture of the ASP and atherothrombosis. In studying the process of atherosclerosis over many years, special attention was paid to the lipid theory, but nowadays there is evidence of immune inflammation. Cytokines play an important role in the development of aseptic inflammation and contribute to the destabilization of the ASP. Inflammatory cytokines impair tissue microcirculation and cause hypoxia, which activates and accumulates free radicals in the ASP.

Method for Determining the Concentration of Lipoproteins in Blood Serum

The parameters of the blood lipid profile were assessed by determining the concentrations of total cholesterol (TC), low-density lipoproteins (LDL), triglycerides (TG), high-density lipoproteins (HDL), and the atherogenic coefficient (AC). Lipid levels were measured using a homogeneous enzymatic colorimetric method with the Hitachi-902 biochemical analyzer. HDL levels were identified in the supernatant following the precipitation of other classes of lipoproteins using dextran sulfate. The concentration of LDL was calculated using the Friedewald formula [168].

LDL = TC – HDL – TG/5

or

LDL (in mmol/L) = TC – HDL – TG/2.2

There are two assumptions underlying this formula:

1. The majority of plasma TG is contained in LDL and chylomicrons (CM);
2. The mass ratio of TG/TC in LDL is 5:1 in mg, and 2.2:1 in mmol.

This formula is not applicable when TG levels exceed 4.5 mmol/L (>400 mg/dL) [38, 107]. The normal value for TC was taken as its content in blood serum <180 mg/dL, HDL >40 mg/dL, and TG <200 mg/dL [38].

The distribution of TC between atherogenic and antiatherogenic lipoproteins was studied using the atherogenic coefficient (AC), which was determined by the following formula:

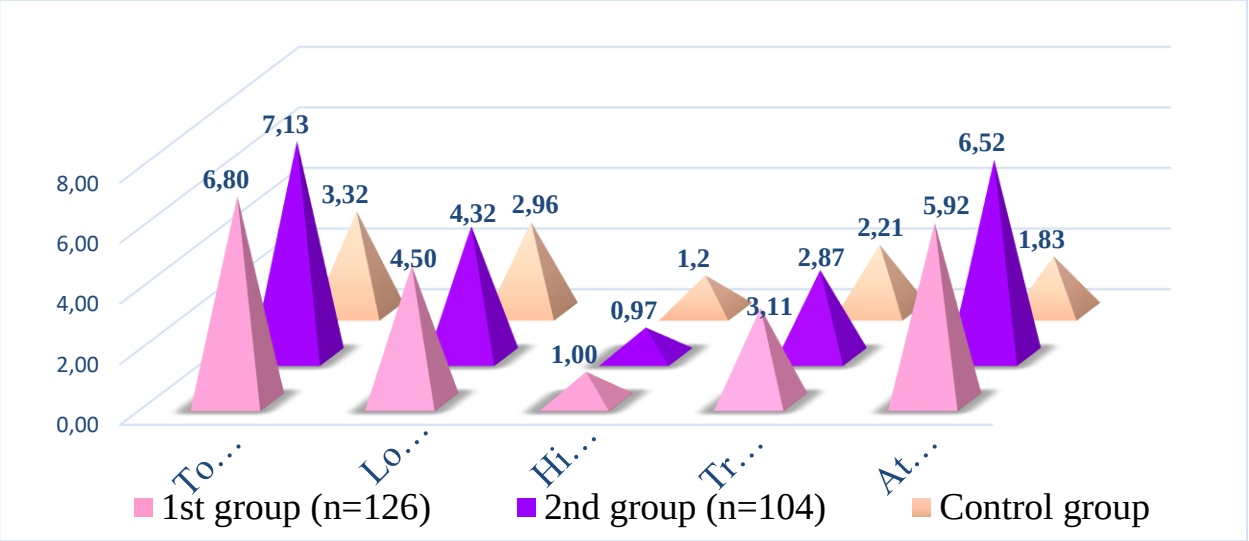
AC = (TC – HDL) / (HDL)

where AC is expressed in relative units (RU). Normally, the atherogenic coefficient is within 2–3 RU. If the atherogenic coefficient is between 3 and 4 RU, there is a moderate probability of developing atherosclerosis. If the value is above 4 RU, there is a high probability of developing atherosclerosis. A value of 7 RU or more indicates strongly expressed atherosclerosis.

Relationship of Lipoprotein Levels in the Blood Depending on the Clinical Manifestation of CAD in Young Men

One of the objectives of the present study is to assess the lipid status in patients with CAD. As a result, we studied the lipid spectrum among patients of young and elderly ages. The study results showed that the levels of TC, LDL, and TG were elevated in both

groups; TC in the second group was increased by 0.33 mmol/L compared to the first group and amounted to 7.13 ± 0.75 mmol/L and 6.8 ± 0.86 mmol/L, respectively ($p < 0.001$*), while in the control group the average TC was 3.32 ± 0.60 mmol/L ($p < 0.001$*). Regarding HDL levels, no statistically significant differences between the groups were found: in the first group, 1.0 ± 0.15 mmol/L, and in the second group, 0.97 ± 0.16 mmol/L ($p = 0.034$*), although this indicator was below normal in the elderly group, while in the control group it was 1.2 ± 0.18 mmol/L ($p < 0.001$*). LDL in the first group was 4.5 ± 0.83 mmol/L, and in the second group it was 4.32 ± 0.62 mmol/L, respectively ($p = 0.038$*), which indicates a disturbance in lipid metabolism in patients with CAD; in the control group, LDL averaged 2.96 ± 0.83 mmol/L ($p < 0.001$*). In patients of the first group, TG was significantly higher and amounted to 3.11 ± 0.92 mmol/L, while in the second group it was 2.87 ± 0.81 mmol/L ($p < 0.0001$*); in the control group, TG was 2.21 ± 0.74 mmol/L ($p < 0.001$*). The AC was elevated in both groups, being 5.92 ± 1.26 in the first group, 6.52 ± 1.2 in the second group, and 1.83 ± 0.8 in the control group ($p = 0.03$) (Figure 4.1).



Conclusion for the chapter

The analysis of lipid profiles in patients with CAD demonstrated that LDL levels in both the first and second groups were similarly elevated in comparison to the control group, measuring 6.8 ± 0.86 mmol/L and 7.13 ± 0.75 mmol/L, respectively. Triglyceride levels were notably higher in the first group, reaching 3.11 ± 0.92 mmol/L, while in the second group this figure was slightly lower at 2.87 ± 0.81 mmol/L. Statistically significant differences were found in lipid indicators based on clinical variants of unstable angina and AMI. Patients with VVS and PSN showed lower levels of atherogenic lipoproteins compared to those with AMI in both young and elderly cohorts. Elevated concentrations of atherogenic lipoproteins and an increased atherogenic coefficient were linked to the early onset of ACS and AMI, underlining the importance of addressing lipid disorders. Timely identification of these risk factors, managing excess body weight, and correcting lipid metabolism disturbances in both young and elderly men are essential for reducing the incidence of cardiovascular complications.

CHAPTER 3.
The role of dyslipidemia in the destabilization of CAD in the working-age individuals

T-lymphocytes contribute to atherogenesis through antigen recognition, proliferation, and initiating cell-mediated inflammation. Their heightened activation is linked to the destabilization of plaques and blockage of coronary arteries. Although elevated immune markers are also present in patients with stable angina, significant T-cell activation is predominantly observed in those with unstable angina and myocardial infarction (MI). Neutrophils, while typically absent in uncomplicated The primary factor contributing to the development of coronary artery disease (CAD) and myocardial infarction (MI) is vascular atherosclerosis. Atherogenesis is a complex biological process involving the interaction of the vessel wall with circulating blood elements, various biologically active compounds, and local hemodynamic disruptions—a concept described in Virchow's triad.

Over 150 years ago, Rudolf Virchow identified three key stages in the progression of atherosclerosis:

1. Initial irritation of the inner vascular lining,
2. Degenerative changes leading to fat and protein accumulation (atheromatous plaque formation),
3. Inflammation, involving connective tissue reactions and immune activation.

Today, our understanding of the disease has advanced beyond the idea that high cholesterol alone causes atherosclerosis. One major turning point was the work of R. Ross, whose study titled "Atherosclerosis – An Inflammatory Process" revealed that atherosclerosis is fundamentally an inflammatory condition. It progresses through a series of cellular and molecular events—from the initial fatty streaks to plaque rupture and the onset of MI.

The inflammatory process begins when endothelial cells become activated. This triggers the expression of adhesion molecules and the release of proinflammatory cytokines and chemokines. Oxidized low-density lipoproteins (LDL) in the subendothelial space also play a key role by releasing phospholipids that further stimulate endothelial cells. Vascular regions experiencing irregular blood flow or reduced shear stress are especially prone to this activation.

Endothelial dysfunction results in increased permeability and adhesion properties, promoting the attachment of white blood cells and platelets. The process of leukocyte adhesion begins with rolling, mediated by selectins, and progresses to firm adhesion through the involvement of integrins and chemokines. This leads to leukocyte arrest and eventual migration through the endothelium—a step called diapedesis.

Molecules such as ICAM-1, ICAM-2, and VCAM-1 assist in the tight binding of leukocytes to the endothelium, preparing for their passage into the tissue. Platelet endothelial cell adhesion molecule-1 (PECAM-1) plays a central role in this migration. Each stage of leukocyte

e, as it initiates processes such as cardiomyocyte apoptosis and myocardial hypertrophy [154].

Another key cytokine is Interleukin-6 (IL-6), which is involved throughout the progression of atherosclerosis—from the initial inflammatory response to plaque rupture. IL-6 activates endothelial cells, promotes platelet-induced thrombosis, drives smooth movement involves a finely coordinated system of molecules, and disrupting any part of this process can impair the body's immune response within the vessel wall.

Multiple types of immune cells participate in the inflammatory response once it is triggered, notably monocytes, T- and B-lymphocytes, and mast cells. Among these, monocytes and macrophages play a central role. Research has shown that macrophages tend to accumulate in the areas of atherosclerotic plaques, are often found in thrombosed plaques following rupture, suggesting they are recruited during acute events.

Macrophages intensify the inflammatory process by releasing various cytokines and growth factors. Several studies have shown that increased levels of cytokines in MI patients are indicators of active inflammation and serve as predictors of adverse cardiovascular outcomes. Cytokines, which are low-molecular-weight proteins facilitating intercellular communication, include interferons, interleukins, chemokines, tumor necrosis factors, colony-stimulating factors, and growth factors. Normally present in minimal amounts in the blood, elevated cytokine levels suggest the presence of disease.

Tumor necrosis factor-alpha (TNF-α) is a major pro-inflammatory cytokine, primarily produced by macrophages and monocytes. It plays a vital role in inflammatory and immune processes and influences lipid metabolism, coagulation, and endothelial function. TNF-α promotes the expression of adhesion molecules by endothelial cells, stimulates chemotaxis, activates immune cells, and enhances prostaglandin synthesis. In atherogenesis, it contributes by inducing cytokine production, activating adhesion molecules, and stimulating various chemoattractants and growth factors.

In terms of lipid metabolism, TNF-α reduces the activity of enzymes such as 7α-hydroxylase and lipoprotein lipase, leading to increased triglyceride production in the liver. Elevated serum TNF-α levels in CAD patients are associated with poor prognosis. Numerous studies report high TNF-α concentrations in individuals with MI. However, it has also been shown that patients with coronary atherosclerosis without acute events may not demonstrate elevated TNF-α levels.

Interleukin-1 (IL-1) is a major proinflammatory cytokine that plays a central role in regulating inflammation and immune responses. It exists in two biologically active isoforms—IL-1α and IL-1β—both of which function through binding to the IL-1 receptor (IL-1R), although they do not have completely identical actions. Once IL-1 binds to its receptor, it triggers the release of various cytokines and chemokines, promotes the expression of adhesion molecules on endothelial cells, and leads to the recruitment of inflammatory cells. IL-1 contributes to endothelial injury, enhances cellular proliferation and differentiation, and stimulates the release of matrix-degrading enzymes [223].

Research has shown that IL-1 can act synergistically with other inflammatory mediators, especially tumor necrosis factor-alpha (TNF-α), resulting in a highly toxic inflammatory response [174]. Together, these cytokines encourage the release of procoagulants, nitric oxide, and myocardial depressant factors by endothelial cells, leading to reduced heart muscle contractility [42]. In the context of atherogenesis, IL-1 promotes vascular inflammation and contributes to the instability of atherosclerotic

plaques. It also plays a role in adverse cardiac remodeling after myocardial infarction (MI) by increasing matrix metalloproteinase activity. Additionally, IL-1 is considered a predictor of heart failurmuscle cell proliferation, and encourages lipid uptake by macrophages [292]. It also attracts neutrophils and macrophages to sites of inflammation and increases the expression of adhesion molecules on endothelial cells [212,268]. Elevated levels of IL-6 and C-reactive protein have been correlated with the extent of myocardial infarction [21, 211, 212]. Additionally, high IL-6 concentrations are often associated with reduced HDL cholesterol levels [203].

Although many studies have confirmed elevated levels of cytokines such as TNF-α, IL-1, IL-6, and IL-10 in patients with MI and CAD, the findings are often inconsistent. Despite the well-established role of proinflammatory cytokines in atherogenesis, there remains variability in the reported data. As such, further investigations are essential to gain a clearer understanding of the mechanisms involved and to improve the prevention and treatment strategies for cardiovascular diseases, especially coronary artery disease and myocardial infarction.

Statistical Data Processing

Statistical data processing was performed using the R Studio statistical software packages (version 3.5.2). Data storage was carried out in a Microsoft Excel 2019 database, and the primary processing was conducted using R Studio 3.5.2 with libraries such as "Epidisplay," "dplyr," among others. The data were presented as the mean (M) ± standard deviation (SD).

To assess the statistical significance of differences in continuous variables, appropriate tests were selected based on the distribution type. For normally distributed data, the Student's t-test was applied, while for data with a non-parametric distribution, the Kolmogorov-Smirnov test and the Mann-Whitney U-test were used.

A level of statistical significance of $p < 0.05$ was applied. After descriptive data analysis, odds ratios (OR) were calculated using generalized logistic regression with 95% confidence intervals. The significance of differences when comparing groups was assessed by the reliability of differences in the frequency distribution of the studied characteristics in the groups, determined using the two-tailed Fisher's exact test.

The statistical analysis of the molecular-genetic studies involved evaluating allele frequencies of genes, genotypes, and their combinations, along with an analysis of contingency tables. Allele and genotype frequencies were calculated using the direct counting method. The association between gene and genotype frequencies was statistically assessed using the odds ratio (OR).

The relationship between the compared variables was determined using a factorial table with the χ^2 test, calculated by the Holdene formula:

$$\chi^2 = W\, y^2$$

taking into account one degree of freedom – df = 1, after which the final formula takes the following form:

χ^2 = [formula]

If at least one of the values a, b, c, d equals 1, then the significance of differences in the frequency of occurrence of genes and haplotypes is calculated using the χ^2 test with Yates' continuity correction:

χ^2 = [formula]

A χ^2 value exceeding 3.841 ($p < 0.05$) is considered an indicator of a significant difference between the frequency characteristics in the compared groups.

CHAPTER 4.
Evaluation of indicators depending on the treatment of patients with CAD in the working-age individuals

Evaluation of Indicators Depending on the Treatment of Young Patients with CAD

At present, therapy for CAD in patients, especially in young individuals, using drugs that affect clinical and hemodynamic parameters is considered a current problem. Recently, despite a significant expansion of the range of medications affecting the clinical course, practical physicians are faced with the equally complex problem of choosing the optimal drug for the treatment of a specific patient.

Among the medications, the comprehensive drug produced domestically, Tivorel, attracted our special interest. Its composition includes the amino acids levocarnitine and arginine hydrochloride. The influence of Tivorel on the clinical course of CAD and lipid metabolism has been insufficiently studied, which makes it one of the pressing issues in modern cardiology. One of the main functions of levocarnitine, which is included in Tivorel, is the transport of fatty acids through the inner membrane into the mitochondrial matrix for ATP production during beta-oxidation. In patients with CVD (CHF, myocardial ischemia, DLP, peripheral vascular diseases) and SD, regardless of their age, an absolute or relative deficiency of levocarnitine is also observed.

The potential mechanisms of the positive effects of levocarnitine in these diseases include increased glucose metabolism through the stimulation of aerobic glycolysis, increased coronary blood flow, and an antiarrhythmic effect, as well as inhibition of free radical production (antioxidant action). Levocarnitine reduces the basal metabolic rate in the human body and slows the breakdown of protein and carbohydrate molecules. Levocarnitine controls the rate of oxidation of long-chain fatty acids as a specific cofactor, facilitating their transport through the inner mitochondrial membrane, and also participates in the removal of their excess from the mitochondria and cytoplasm.

Another component of Tivorel is L-arginine, which is a valuable amino acid that positively influences the cardiovascular system by maintaining an optimal level of cholesterol in the blood and significantly reducing fat deposits. In addition, L-arginine contributes to increasing collateral blood flow to the occluded coronary vessel, thereby improving the overall condition of patients with CAD, reducing the frequency of angina attacks, decreasing the number of nitrate doses taken, enhancing the patients' tolerance to physical exertion, improving the rheological properties of blood, preventing the formation of blood clots, and significantly reducing the risk of thrombosis and atherosclerotic plaque (ASP) formation.

Tivorel contains the amino acids levocarnitine and arginine hydrochloride. It is manufactured as an infusion solution in 100 ml vials for intravenous administration.

Each ml of the solution contains: arginine hydrochloride – 42 mg, levocarnitine – 20 mg; excipient: water for injections.

Prior to hospitalization, patients in outpatient conditions were taking:

- Aspirin in a dose of 75–125 mg/day: Group 1 – 20 (43.5%), Group 2 – 47 (90.4%).
- β-adrenoblockers (bisoprolol) 5 mg/day: Group 1 – 15 (32.6%), Group 2 – 40 (80%).
- Nitrates: Group 1 – 12 (26%), Group 2 – 20 (40%).
- ARB II: Group 1 – 6 (13%), Group 2 – 17 (33.6%).

Anticoagulant therapy was carried out using unfractionated heparin under the control of activated partial thromboplastin time, followed by the administration of low molecular weight heparins for 5–7 days. The average duration of hospitalization was 9.6 ± 2.7 days (Table 3.1.3).

Таблица 3.1.3

Groups of medications	**1st group (n=46)**	**2nd group (n=50)**
	Frequency6 of use (%)	
Nitratres	12(26.%)	20 (40%)
Betta-blockers	15(32.6%)	40 (80%)
ARAs medications	6 (13%)	17 (33.6%)
Antiplatelet agents	20 (43.5%)	47 (90.4%)
Statins	16 (34.7%)	36 (72%)

Patients selected by random sampling were divided into 2 groups. The 1st group consisted of 65 (59%) (35 men and 30 women) with CAD, who received conventional traditional therapy (CTT). The 2nd group included 45 (41%) (25 men and 20 women), who, in addition to traditional therapy, received the drug tivorel at a dose of 100 ml/day intravenously for 5 days, followed by a transition to L-carnitine tablets at 500 mg twice a day for 1 month. The duration of observation was 6 months. Traditional therapy included intravenous infusion of nitrates for 12–24 hours, followed by prolonged-release nitrate tablets, antiplatelets, anticoagulants, cardioprotectors, beta-blockers, ACE inhibitors or ARA group drugs, as well as statins.

The conducted studies showed that after 30 days of CTT and treatment including tivorel, unidirectional changes in biochemical parameters in the blood of patients with CAD were recorded.

When studying the dynamics of the clinical condition of patients with CAD before and after treatment, it was found that in the 1st group, the average number of angina attacks decreased from 6.8 to 4.9 times a day, while in the 2nd group, the number of angina attacks decreased from 7.1 to 2.4 times a day. The average number of angina attacks decreased by 27% in the 1st group and by 86% in the 2nd group (see Fig. 3.4.1).

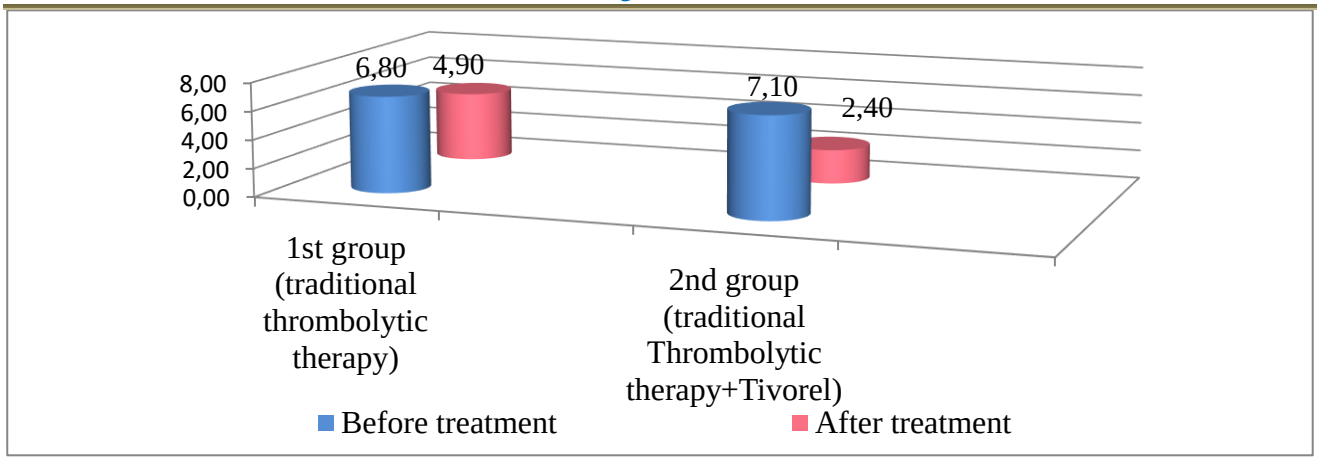


Fig. 3.4.1. Dynamics of angina attacks before and after treatment over 24 hours.

When studying the number of nitroglycerin tablets consumed over 24 hours by patients with CAD before and after treatment in the studied groups, the following data were obtained: in the 1st group, the average number of nitroglycerin tablets consumed decreased from 6.1 to 3.9 times a day, while in the 2nd group, it decreased from 7.0 to 2.4 times a day (see Fig. 3.4.2). In the studied group, the average number of nitroglycerin tablets consumed to relieve angina pain decreased by 1.5 times in the 1st group and by 2.9 times in the 2nd group.

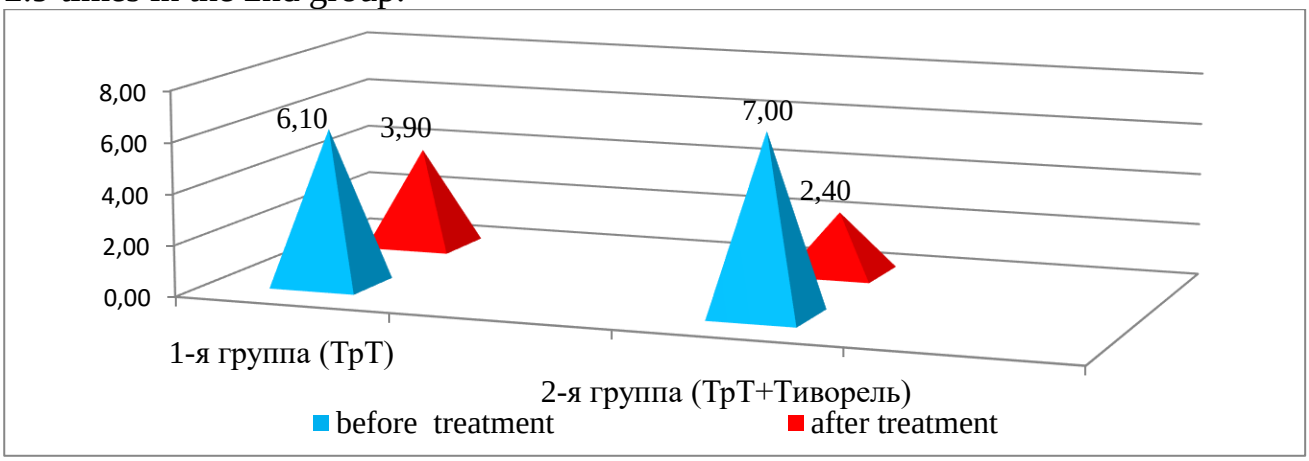


Fig. 3.4.2. Dynamics of nitroglycerin tablet consumption before and after treatment over 24 hours.

In young men receiving CTT, the total cholesterol (TC) decreased by 5.9 mmol/L, while in patients receiving CTT + Tivorel, it decreased by 5.38 mmol/L ($p < 0.001$*). The levels of LDL decreased by 0.88 mmol/L or more in patients receiving CTT + Tivorel, with values of 3.74 and 3.1 mmol/L, respectively ($p < 0.001$*). HDL in patients receiving CTT increased to 1.1 mmol/L, while in patients receiving CTT + Tivorel, it increased to 1.6 mmol/L ($p < 0.01$*). Triglycerides (TG) decreased the most in patients receiving CTT + Tivorel, with values of 1.69 mmol/L and 2.5 mmol/L, respectively ($p = 0.04$*). The atherogenic index (AI) decreased to 4.2 in patients receiving CTT and to 3.14 in patients receiving CTT + Tivorel ($p < 0.001$*) (see Table 3.4.1).

Table 3.4.1

Lipoprotein levels in young men depending on the therapy admimistrated .

Lipoprotein indicators	Traditional treatment n=30 (mol/l)	Traditional treatment +Tivorel n=35 (mmol/l)	Mann-Whitney-Wilcoxon test
Total cholesterol	7,14	7,1	p=0,049
Total cholesterol after treatment	5,9	5,38	<0,001*
Low density lipoproteins before treatment	4,5	4,2	p<0,001
Low density lipoproteins after treatment	3,66	2.9	p<0,001*
High density lipoproteins before treatment	1,0	1,1	p=0,03
High density lipoproteins after treatment	1,2	1.6	p<0,01*
Triglycerides before treatment	3,62	3,19	P<0,001
Triglycerides after treatment	1,62	2,5	0,004*
Atherogenetic coefficient before treatment	5,88	5,9	p=0,03
Atherogenetic coefficient before treatment	4,2	3,14	<0,001*

In young women undergoing traditional therapy (CTT), total cholesterol (TC) decreased by 6.35 mmol/L, while those receiving CTT + Tivorel experienced a reduction of 5.38 mmol/L ($p < 0.001$*). The decrease in low-density lipoproteins (LDL) was 0.69 mmol/L greater in the CTT + Tivorel group, with values of 3.8 and 3.01 mmol/L, respectively ($p < 0.01$). High-density lipoproteins (HDL) increased to 2.2 mmol/L in the CTT + Tivorel group, while it increased to 1.3 mmol/L in the CTT-only group ($p < 0.008$). The reduction in triglycerides (TG) was most pronounced in the CTT + Tivorel group, with a value of 1.7 mmol/L compared to 2.8 mmol/L in the CTT group ($p < 0.004$*)

The atherogenic index (AI) decreased to 4.45 in women receiving CTT and to 3.3 mmol/L in those receiving CTT + Tivorel ($p < 0.003$*) (see Table 3.4.2).

Table 3.4.2

Lipoprotein indices in young women depending on the therapy administrated

Lipoproteins indicators	Traditional treatment n=20 (mol/l)	Traditional treatment +Tivorel n=25 (mmol/l)	Mann-Whitney-Wilcoxon test
Total cholesterol	6,88	7,1	0,07
Total cholesterol after treatment	6,35	5,38	<0,001*
Low density lipoproteins before treatment	4,42	4,13	0,75
LowЛПВП до лече density lipoproteins after treatment	3,8	3.01	<0,01*
High density lipoproteins before treatment	0.96	1.03	0,2
High density lipoproteins after treatment	1,3	2.2	<0,01*
Triglycerides before treatment	3,1	3,19	0,33
Triglycerides after treatment	1,7	2,8	0,004*
Atherogenetic coefficient before treatment	6,3	6,42	0,35
	4,45	3,3	<0,001*

When studying the ECG, the elevation of the ST segment among patients in the 1st group changed from 33% to 15.7%. In the 2nd group, this indicator decreased from 31% to 9.9%. T-wave inversion was observed in young patients from 39% to 15.2% of cases, while in the 2nd group, it was present in 38% to 8.7% of cases (see Fig. 3.4.3).

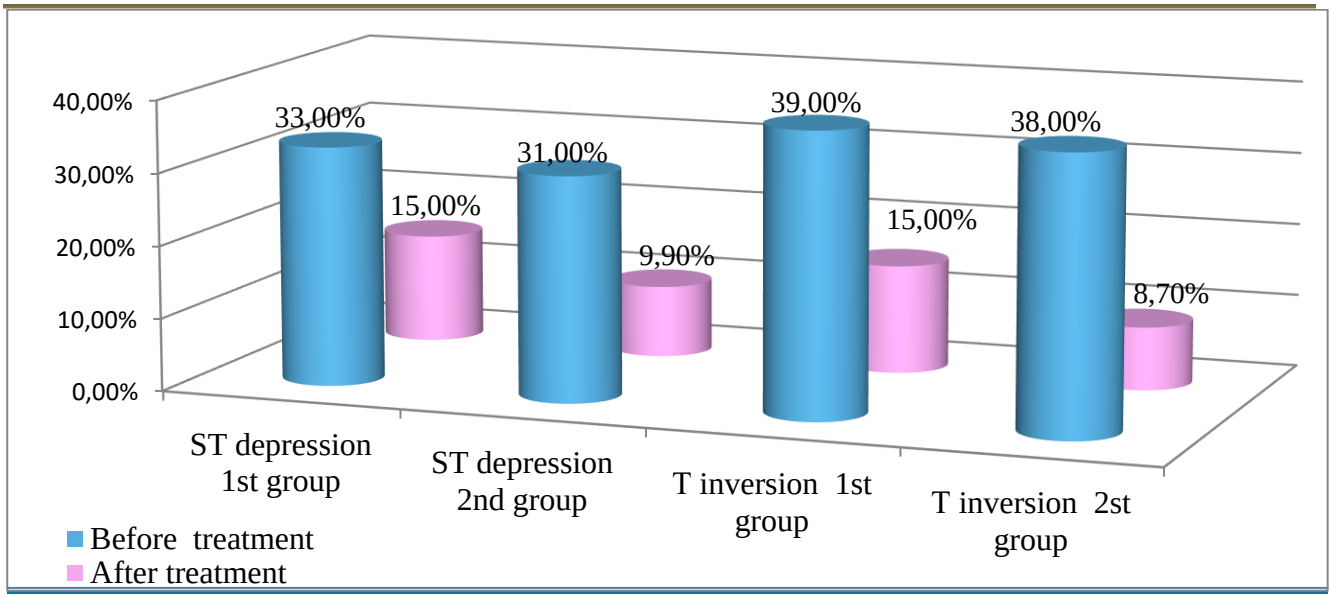


Fig. 3.4.3. Dynamics of ECG indicators before and after treatment in patients with CAD

When studying the echocardiography (ECHO) data, the following results were obtained: the left ventricular ejection fraction (LVEF) among patients in the 1st group changed from 51.6% to 54.7%, while in the 2nd group, this indicator ranged from 50.3% to 55.2%. The area of hypokinesis decreased from 35% to 15.2% of cases, while in the 2nd group, it was observed from 37% to 9.7% of cases (see Fig. 3.4.4).

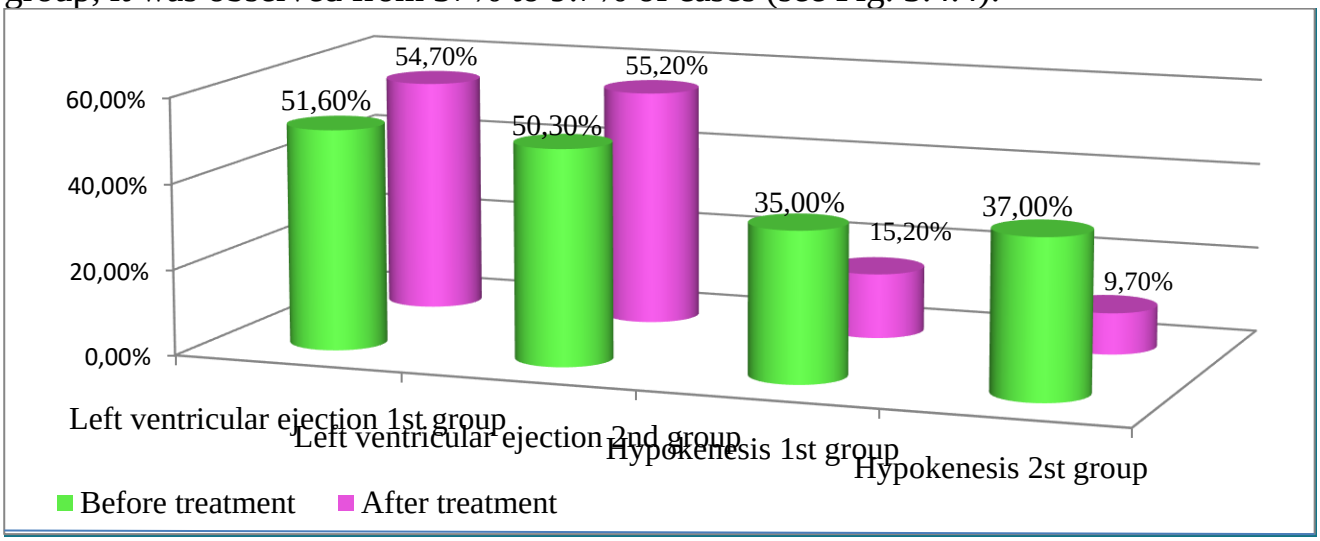


Fig. 3.4.3. Dynamics of ECHO indicators before and after treatment in patients with CAD

In young male and female patients, the most significant improvements were observed in those receiving CTT + Tivorel. For patients on CTT alone, there were no substantial changes in the levels of total cholesterol (TC), low-density lipoproteins (LDL), high-density lipoproteins (HDL), or triglycerides (TG) by the end of treatment. However, patients who received Tivorel alongside traditional therapy showed statistically significant positive changes in anginal pain frequency, nitroglycerin usage, as well as improvements in ECG and ECHO parameters. These findings suggest that adding Tivorel to traditional therapy may enhance treatment outcomes, improve prognosis, and elevate the quality of life for young patients.

FINDINGS

1. Young patients with CAD often share the same risk factors (smoking, stress, excess body weight, family history, hypertension, poor nutrition, alcohol and energy drink consumption, etc.) as older patients with CAD. This allows them to be considered potential candidates for an earlier and more severe course of coronary artery disease in the future.
2. The lipid profile analysis among patients with CAD showed that LDL and TG levels were significantly higher in men with CAD compared to patients with stable angina (by 0.38 mmol/L and 0.43 mmol/L, respectively). Elevated levels of atherogenic lipoproteins contributed to the early development of acute coronary syndrome (ACS) and myocardial infarction (MI), which is an important factor for correcting these disorders.
3. Thus, the most common risk factors between both groups were considered to be smoking, hypertension, diabetes, and excess weight. In women, the most significant factors in the development of CAD were hypertension, excess weight, and obesity. In men, the primary factors leading to the development of CAD were stress, smoking, and alcohol consumption.
4. In studying the lipid profile of the blood, an increase in LDL, total cholesterol, and triglyceride levels was observed in both groups. No statistically significant differences were found between the groups regarding HDL levels.
5. According to ECG data, young men with CAD showed a higher degree of damage to the anterior and posterior walls compared to female patients.
6. Thus, ECHO data indicated that ischemic damage to more than one wall was more frequently observed in young men than in women. The identification of this information indicates that the disease can have a particularly severe course in younger individuals and requires timely and rational treatment, as it may lead to early disability and mortality.

CONCLUION

According to the WHO, atherosclerotic cardiovascular diseases (CVD) are among the leading causes of death worldwide, with projections suggesting that by 2030, CVD-related mortality may reach approximately 23.6 million. Ischemic heart disease (IHD) is the most prevalent form of CVD, accounting for over 50% of cases. In Russia, around 20% of young patients with IHD die prematurely, leading to significant economic losses. In recent years, there has been a concerning trend towards younger populations developing IHD, including unstable forms of angina. This is especially alarming since young people represent the active workforce and the productive backbone of society, crucial to the socio-economic future of any nation.

While traditional modifiable and non-modifiable risk factors (RF) are known to contribute to the development of IHD, the role of these factors in young men remains a subject of ongoing debate. Our study found that all traditional modifiable risk factors contribute to the onset of IHD in young men. Furthermore, many young patients also have comorbidities that may worsen the progression of the disease.

Our research revealed that the prevalence of traditional RF in young and older men was the same, indicating the necessity for monitoring and timely correction of modifiable RF regardless of age, as well as directing efforts towards increasing medical awareness.

Among modifiable RF, dyslipidemia associated with excess weight plays a special role in increasing the risk of developing CVD. According to several epidemiological studies, 26.6% of men aged 35 to 44 suffer from obesity. Other studies have established that the risk of developing IHD, hypertension (HT), and diabetes significantly increases with a body mass index (BMI) of 25 kg/m² or higher. At a BMI of more than 30 kg/m², mortality from CVD is 1.5-2 times higher compared to patients with normal body weight. The frequency of coronary complications increases by 10% with each unit increase in BMI, and an increase in BMI from 20 to 30 kg/m² contributes to a 10-20 mg/dL increase in LDL concentration.

In our study, when analyzing the nature of lipid metabolism disorders in the examined groups, it was found that the LDL level in the first group was 4.5 mmol/L, while in the second group it was 4.32 mmol/L. The triglyceride levels in the first group were significantly higher at 3.11 mmol/L, compared to 2.21 mmol/L in the second group. The lipid profile indicators according to the clinical variants of unstable angina and myocardial infarction (MI) were statistically significant; patients with newly developed and progressive angina had lower atherogenic lipoprotein levels compared to those with MI, both in young and older age groups. High levels of atherogenic lipoproteins and atherogenic coefficient indicators contributed to the early development of acute coronary syndrome (ACS) and MI, which is important for correcting these disorders.

IHD is a disease that arises from inadequate oxygen supply to the myocardium due to atherosclerosis of the coronary arteries, spasm of intact coronary arteries, microcirculation disorders, or hypercoagulation of the blood composition.

Atherosclerotic changes are considered a chronic inflammatory disease characterized by an immune response to endothelial wall damage due to lipid metabolism disorders.

Inflammatory processes play a significant role in the development of the atherosclerotic focus and destabilization of atherosclerotic plaques, which contribute to thrombus formation and related complications in coronary arteries. L-arginine hydrochloride suppresses the synthesis of endothelin-1, preventing vasoconstriction and improving coronary circulation.

In our study, we examined the relationship between several risk factors and the progression of coronary heart disease in young men, particularly lipid profile indicators. When investigating cytokine levels in relation to LDL levels, it was found that patients with ischemic heart disease in both young and elderly age groups who had high LDL levels (above 4.0 mmol/L) exhibited statistically significant levels of pro-inflammatory interleukin, i.e., IL-1β increased to 70.13±0.7 pg/mL and 80.2±0.5 compared to patients with low LDL levels (below 4.0 mmol/L) whose IL-1β levels were elevated to 65.2±8.15 and 74.7±9.7 pg/mL ($p1<0.0023^*$, $p2<0.0063^*$). Additionally, patients with high LDL levels (above 4.0 mmol/L) had statistically significant levels of anti-inflammatory interleukin, i.e., IL-10 decreased to 12.6±1.56 and 11.3±1.58 pg/mL compared to patients with low LDL levels (below 0.5 mmol/L) whose IL-10 levels were reduced to 13.6±1.58 and 11.8±1.16 pg/mL ($p1<0.001^*$, $p2<0.042^*$). Early detection of these risk factors, combating excess weight, and timely treatment of lipid and cytokine imbalance in young and elderly men contribute to reducing the development of cardiovascular diseases.

Currently, according to WHO data, diseases of the cardiovascular system with an atherosclerotic genesis are one of the main causes of mortality in the population, and WHO forecasts suggest that by 2022, mortality from cardiovascular diseases may reach around 22.4 million people. Among cardiovascular diseases, ischemic heart disease occupies a leading position and is responsible for more than 45% of mortality cases.

IHD is a disease that occurs due to inadequate oxygen supply to the myocardium as a result of coronary artery atherosclerosis, spasm of intact coronary arteries, microcirculation disorders, or hypercoagulation of blood composition. Atherosclerotic changes are considered a chronic inflammatory disease characterized by an immune response to endothelial wall damage due to lipid metabolism disorders. Inflammatory processes play an important role in the development of the atherosclerotic focus and destabilization of atherosclerotic plaques, which contribute to thrombus formation and related complications in coronary arteries.

Our research revealed that the prevalence of traditional risk factors for atherosclerosis was similar in both young men and women. This highlights the importance of monitoring and promptly addressing modifiable risk factors, irrespective of gender or age, and emphasizes the need to increase medical awareness.

Lipid metabolism disorders and dyslipidemia are crucial risk factors for the development of atherosclerosis and its complications. Every year, more than a million people globally die from cardiovascular diseases, with ischemic heart disease (IHD) accounting for over half of these deaths. Young individuals, being the main active workforce and the productive resources of society, play a critical role in determining the socio-economic prospects of any nation. Given the alarming trend of earlier onset of coronary heart disease, which often leads to fatal outcomes, it is essential for healthcare

systems to focus on understanding the clinical progression of this disease and addressing the risk factors in young patients.

Among the modifiable risk factors, dyslipidemia linked to excess weight is particularly significant, as it heightens the risk of developing cardiovascular diseases. Several epidemiological studies have shown that 15.4% of men and 15.6% of women aged 35 to 44 are affected by grade I obesity. Other studies have demonstrated that the likelihood of developing IHD, hypertension, and diabetes significantly increases with a BMI of 25 kg/m2 or higher. Moreover, individuals with a BMI exceeding 30 kg/m2 face 1.5 to 2 times higher mortality from cardiovascular diseases compared to those with normal weight. The frequency of coronary complications increases by 15% with every unit increase in BMI, and a rise in BMI from 25 to 30 kg/m2 leads to an increase in LDL concentration by 15-25 mg/dL.

At the same time, in our study, when analyzing the nature of lipid metabolism disorders in the examined groups, it was found that the LDL level in the first group was 4.5 mmol/L, in the second group it was 4.42 mmol/L. The triglycerides in patients in the first group were significantly higher at 3.62 mmol/L, while in the second group it was 3.1 mmol/L. The lipid profile indicators by clinical variants of unstable angina and IHD were statistically significant, as patients with newly onset and progressive angina had lower atherogenic lipoproteins compared to those with IHD in young age.

Based on our study, a comparative analysis of the leukocyte formula of patients with coronary heart disease (CHD) from different age groups revealed statistically significant differences in both the percentage content and the absolute number of monocytes (8.0 vs. 7.0, $p = 0.025$ and 0.90 vs. 0.70, $p = 0.022$, respectively).

When studying the indicators of the general biochemical blood analysis, it was noted that in female patients, the glomerular filtration rate (GFR) was 8.1 ml/min lower compared to male patients, averaging 80.4±10.5 ml/min and 88.5 ml/min, respectively ($p < 0.0001$). In the control group, the average GFR was 99.8±18.5 ml/min ($p = 0.26$).

Regarding the localization of ischemic changes on the ECG, the following observations were made: In the first group, ischemic changes in the anterior wall were observed in 27 (41.5%) patients, while in the second group, 15 (33.3%) patients exhibited these changes ($p = 0.99$). Ischemia in the posterior wall of the left ventricle (LV) was noted in 26 (40%) patients in the first group, while in the second group, 17 (37.8%) patients had this finding ($p = 0.45$). Ischemic changes in the anterior-septal wall were observed in 7 (15.6%) patients in the second group, which was twice the frequency seen in the first group (7 or 10.8%); however, this difference was not statistically significant ($p = 0.14$). Ischemia of the lateral wall was found in 5 (7.8%) patients in the first group and in 6 (13.3%) patients in the second group ($p = 0.81$). Ischemia involving two or more walls was present in 28 (43.1%) patients in the first group and 19 (42.2%) patients in the second group ($p = 0.79$).

Echocardiographic (ECHO) results showed the following changes in the groups: The left ventricular ejection fraction (LVEF) in the first group averaged 53.6%, while in the second group, it decreased to 50% ± 8.4 ($p < 0.01$). In the control group, the average LVEF was 56% ± 9.0 ($p = 0.48$). The end-diastolic volume (EDV) in the first group averaged 140.3 ± 40.0 ml, while in the second group, it was 152 ± 49.03 ml ($p = 0.09$),

with the control group having an average of 120 ± 20.2 ml ($p < 0.05$). The end-systolic volume (ESV) was 78.7 ± 25.2 ml in the first group, 84.6 ± 36.2 ml in the second group ($p = 0.11$), and 56 ± 14.4 ml in the control group ($p < 0.001$).

A single zone of hypokinesis was observed in 30 (46.2%) patients in the first group and 22 (48.9%) patients in the second group ($p = 0.78$). Hypokinesis in more than two zones was present in 35 (53.8%) patients in the first group and 23 (51.1%) patients in the second group ($p = 0.01$). Akinesis was identified in 24 (36.9%) patients in the first group and 15 (45.5%) patients in the second group ($p = 0.01$). No zones of hypo- or akinesis were detected in the control group according to ECHO data.

The conducted studies indicated that dyslipidemia in young men and women with coronary heart disease (CHD) is a significant prognostic factor for disease progression. The inclusion of Tivorel in the standard treatment regimen significantly reduces total cholesterol, LDL, and triglyceride levels, increases HDL, and improves therapy effectiveness. This approach lowers the risk of adverse prognosis and outcomes in young patients with CHD. Therefore, it is recommended to incorporate these agents into the standard therapy regimen for managing dyslipidemia and lipid imbalances in patients with CHD, improving treatment outcomes, prognosis, and the quality of life for patients.

PRACTICAL RECOMMENDATIONS

1. Patients with coronary heart disease (CHD), both in young and elderly age groups, are advised to undergo immunological assessments to evaluate cytokine imbalances and their correlation with the severity of the disease.
2. To improve the effectiveness of comprehensive prevention for coronary heart disease (CHD) in individuals under 44 years of age, it is crucial to first normalize body weight and working conditions, while also preventing smoking, alcohol consumption, and disorders in lipid metabolism.
3. When it comes to the early detection of CHD, it is important to remember that the disease cannot be diagnosed solely based on clinical signs. Therefore, we must not overlook even the smallest details.
4. To assess the prognosis in young patients with CHD, it is necessary to conduct a dynamic evaluation of electrocardiographic indicators, the condition of heart cavities and structures, as well as the systolic and diastolic functions of the left ventricle during the early stages of the disease (acute and chronic phases) for early diagnosis of complications.

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russjcardiol.elpub.ru (https://doi.org/10.15829/1560-4071-2020-1-3407)

TABLE OF CONTENT

FOR NOTES

KHASANJANOVA F.O.

DIFFERENTIATED APPROACH TO THE DIAGNOSIS AND TREATMENT OF CORONARY HEART DISEASE DESTABILIZATION IN WORKING-AGE MAN

Monograph

PUBLISHER "TIBBIYOT KO'ZGUSI"

Responsible Editor —
Proofreader —
Technical Editor —
Design and Layout —

Printed at the printing house of Samarkand State Medical University
140100, Samarkand, Amir Temur Street, 18.

Signed for printing: ??.2020
Protocol: ?

Format: 60x84 1/16. Font: "Times New Roman".
Printed sheets: ?
Print run: 500 copies. Order No: ?

Phone/Fax: 0(366)2330766
E-mail: samgmu@mail.ru
Website: www.sammu.uz