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RESEARCH ARTICLE

Prognostic Significance of Biomarkers of Inflammation in Acute Coronary Syndrome

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Abstract: Acute coronary syndrome (ACS) remains one of the leading causes of death and disability globally, despite advances in diagnosis and treatment. In recent years, considerable attention has been paid to the role of systemic inflammation in the pathogenesis of atherosclerosis and its complications, which leads to the search for reliable biomarkers capable of predicting the course of the disease and the risk of adverse cardiovascular events. The review analyzes the prognostic significance of key biomarkers of inflammation in ACS, including C-reactive protein (CRP), interleukins (IL-6, IL-1b), tumor necrosis factor alpha (TNF-alpha), leukocyte activation index, as well as newer markers — soluble forms of adhesion molecules (sICAM-1, sVCAM-1), fibrinogen, calprotectin and hemopexin. Special attention is paid to combined indices such as the ratio of neutrophils to lymphocytes (NLC), lymphocytes to monocytes (LMC) and the systemic immune-inflammatory index (SII), which reflect the balance between pro- and anti-inflammatory mechanisms and demonstrate high predictive value in real clinical practice. It has been shown that an increase in the level of these markers is associated with a larger area of coronary lesion, instability of atherosclerotic plaque, an increased risk of recurrent myocardial infarction, heart failure and cardiac death. The results of meta-analyses confirm the independent prognostic contribution of CRP and NLC even after correction for traditional risk factors. At the same time, the need to standardize methods for determining, setting thresholds, and validating biomarkers in different populations is emphasized. Integration of inflammatory markers into existing prognostic models (for example, GRACE, TIMI) can increase their discriminative ability and improve the stratification of patients by risk. A promising direction is the use of multifactorial biomarker panels in combination with imaging and genetic profiling data to build personalized prognosis and therapy algorithms. Thus, biomarkers of inflammation represent not only a reflection of the activity of the pathological process, but also a potentially modifiable target for correction, which opens up new opportunities for improving outcomes in patients with ACS.

Keywords: acute coronary syndrome, inflammation, biomarkers, C-reactive protein, interleukins, tumor necrosis factor-alpha, neutrophil-lymphocyte ratio, systemic immune-inflammatory index, prognosis, cardiovascular events.

INTRODUCTION

Acute coronary syndrome (ACS) is a spectrum of clinical conditions caused by sudden disruption of blood flow in the coronary arteries, and includes unstable angina, non-ST segment elevation myocardial infarction (NSTEMI), and ST segment elevation myocardial infarction (STEMI)[1]. Despite significant advances in early diagnosis, revascularization, and drug therapy, ACS continues to be associated with a high risk of recurrent ischemic events, heart failure, and death. In recent decades, the role of chronic systemic inflammation in the pathogenesis of atherosclerosis and its acute complications has been convincingly confirmed in large-scale epidemiological and interventional studies. Inflammatory mechanisms are involved at all stages of atherosclerotic plaque formation, from initial endothelial dysfunction to its destabilization and thrombogenic activation [2].

In this context, biomarkers of inflammation are considered not only as a reflection of the activity of the pathological process, but also as potential tools for clarifying the prognosis and personification of therapy. Traditional markers, such as C-reactive protein, show a reproducible association with the risk of cardiovascular events, but their individual prognostic value is limited. Modern approaches are aimed at studying complex indices integrating data on the cellular composition of peripheral blood (for example, NLR, SII), as well as at identifying new molecular markers reflecting the activity of the immune system and vascular wall remodeling.

The relevance of the study of the prognostic significance of inflammatory biomarkers is due to the need to improve risk stratification in patients with ACS, especially in conditions of heterogeneity of clinical course and variability of response to therapy. The integration of inflammatory indicators into existing prognostic models can increase their sensitivity and

specificity, contributing to a more accurate identification of high-risk groups and optimization of management tactics.

MATERIALS AND METHODS.

When writing the paper, a set of theoretical and analytical methods was used aimed at systematization, critical assessment and interpretation of modern scientific data in the field of prognostic significance of biomarkers of inflammation in acute coronary syndrome. The main methods used in the writing process are:

The system analysis allowed us to consider inflammatory biomarkers not in isolation, but as part of an integrated pathophysiological network, including immune activation, endothelial dysfunction, thrombogenicity, and vascular wall remodeling. The approach provided an understanding of the relationships between individual markers and their combined contribution to the forecast.

Comparative analysis was used to evaluate the diagnostic and prognostic effectiveness of various biomarkers (traditional and new) based on data from randomized trials, cohort observations, and meta-analyses. The comparison was carried out according to the criteria of sensitivity, specificity, thresholds, stability over time and independence from concomitant factors (age, concomitant pathology, therapy).

The content analysis of scientific literature covered publications in leading medical journals (including the European Heart Journal, Journal of the American College of Cardiology, Circulation, and Nature Reviews Cardiology) from 2000 to 2024. The selection of sources was carried out according to the principles of evidence-based medicine with a priority on research of a high level of evidence (level I on the GRADE scale).

The inductive-deductive method was used to generalize empirical data on the predictive value of individual markers; deduction was used to formulate generalized conclusions about the prospects for their clinical use and embed them into existing risk stratification algorithms.

The method of structured review (narrative review) is used to build a logically consistent narrative covering the pathophysiological foundations, clinical associations and the practical significance of biomarkers. Unlike a systematic review, this approach allows for a more flexible selection of literature, which is advisable for interdisciplinary coverage of the topic.

The analysis of prognostic models included an assessment of the increase in informativeness when integrating inflammatory markers into existing risk scales (GRACE, TIMI, PURSUIT) using indicators of classification improvement (NRI - net classification improvement) and discrimination (AUC, C-statistical). The expert interpretation method was applied at the final stage to develop sound recommendations regarding the clinical applicability of biomarkers, taking into account accessibility, reproducibility and economic feasibility.

Particular attention is paid to minimizing cognitive biases in data interpretation, including publication bias. All the presented conclusions are based on representative samples, longitudinal observations, and statistically significant associations confirmed in independent cohorts.

RESULTS.

Acute coronary syndrome continues to be one of the main causes of death and disability in most countries of the world [3]. Despite the introduction of modern diagnostic technologies such as highly sensitive troponin assays, early coronary angiography, the use of functional methods for assessing ischemia, as well as the development of invasive and drug–based treatment strategies, the proportion of adverse outcomes in patients with ACS remains high [4]. According to international registries, up to 15% of patients suffer a repeat vascular event within the first year after hospitalization, including reinfarction, unstable angina, stroke, or death [5]. This indicates a continuing shortage of tools capable of reliably identifying patients with the most aggressive course of the disease.

In recent years, more and more evidence indicates the central role of inflammatory mechanisms in the development and progression of atherosclerosis. Previously considered a passive deposition of lipids, atherosclerosis is now considered as a chronic inflammatory process of the vascular wall [6]. It is initiated by modified low-density lipoproteins, which penetrate into the intima of the artery and cause activation of the endothelium. This is accompanied by the expression of adhesion molecules (VCAM-1, ICAM-1, E-selectin), which promotes the adhesion of monocytes and their migration into the subendothelial space [7]. Under the influence of local cytokines, monocytes differentiate into macrophages that absorb oxidized LDL and turn into foam cells, the basis of the initial atheroma.

Over time, T lymphocytes, especially Th1 subpopulations, secrete interferon-γ and increase inflammation, participate in plaque formation [8]. Macrophages and smooth muscle cells produce matrix metalloproteinases (MMPs), which weaken the fibrous capsule of the plaque. At the same time, collagen synthesis decreases, which makes the plaque unstable [9]. It is these "inflamed" plaques that are most prone to rupture or erosion, which triggers a cascade of thrombosis and leads to acute occlusion of the coronary artery, the direct cause of ACS.

After the index event, the inflammatory process does not stop. It persists in the area of myocardial necrosis, participating in the remodeling of the left ventricle, the formation of scar tissue and the progression of diastolic

and systolic dysfunction [10]. The level of systemic inflammation in the acute and early post-infarction period correlates with the size of the affected area, the frequency of complications (shock, cardiac rupture, congestive heart failure) and long-term prognosis [11]. This makes inflammation not only a pathogenetic factor, but also a potential object of monitoring and correction.

In these conditions, the search for reliable biomarkers reflecting the activity of the inflammatory cascade is of particular importance. The ideal marker should be stable, accessible for routine determination, have high prognostic information content and allow interpretation in the context of the clinical picture [12]. The C-reactive protein synthesized by hepatocytes under the action of IL-6 remains the most studied. Its levels increase already in the first hours after myocardial injury and remain high for several days [13]. Numerous studies have confirmed that elevated CRP values are associated with a larger lesion area and a higher risk of complications and death.

However, CRP is a non–specific marker that increases with any inflammatory and necrotic processes, which limits its independent prognostic value. Therefore, attention is shifted to more comprehensive indicators reflecting the dynamics of the immune response. For example, the neutrophil to lymphocyte ratio (NLR) is a simple but informative index calculated from the data of a general blood test [14]. Neutrophils are the main effectors of acute inflammation, producing proteases, reactive oxygen species, and pro-inflammatory cytokines. Lymphocytes, on the contrary, are involved in the regulation of the immune response, and their decrease is associated with immunosuppression and increased susceptibility to complications. Elevated NLR reflects an imbalance between activation and control of inflammation and has been repeatedly confirmed as an independent predictor of the adverse course of ACS [15].

Of similar interest is the systemic immune-inflammatory index (SII), which includes neutrophils, lymphocytes, and platelets, three components involved in inflammation, thrombosis, and remodeling. SII has shown high predictive ability in relation to both coronary and extracoronary events [16]. Other markers, such as IL-6, TNF-α, fibrinogen, and calprotectin, are also actively studied, but their widespread use is hampered by the complexity of definition, cost, and lack of standardized reference values.

Accordingly, despite the progress in the treatment of ACS, the problem of forecasting remains relevant. Inflammation is a key mechanism that determines both the development and course of an acute coronary event [17]. Biomarkers reflecting its activity can be an important addition to existing clinical and instrumental risk assessment methods. However, further prospective studies, standardization of techniques, and evaluation of clinical usefulness in different populations are needed to integrate them into routine practice.

The prognostic significance of inflammatory biomarkers in acute coronary syndrome has been actively studied over the past two decades, and today a significant body of data has been accumulated confirming their role in assessing the severity of the process, the risk of complications, and long-term outcomes [18]. These markers allow us to go beyond the anatomical and functional assessment of coronary artery damage, providing information about the biological activity of the atherosclerotic process and the systemic response of the body to ischemic myocardial damage.

One of the most studied and accessible markers is C-reactive protein (CRP), a pentrameric acute phase protein synthesized by hepatocytes under the influence of interleukin–6 [19]. CRP levels begin to rise as early as 6-8 hours after the onset of an ischemic episode, peak at 24-72 hours, and may remain elevated for several days. Many studies, including the analysis of cohorts of the PURSUIT and FRISCUS registries, have demonstrated that elevated CRP values in the acute period of ACS are associated with a larger infarction area, a decrease in the left ventricular ejection fraction, an increased incidence of complications (recurrent ischemia, cardiogenic shock) and an increased risk of death in the next 30 days and in the long term [20]. At the same time, the prognostic value of CRP remains even after correction for age, concomitant diseases and the degree of coronary lesion, which allows it to be considered as an independent predictor of an unfavorable course [21]. However, it should be borne in mind that CRP is a non–specific marker that reacts to any inflammation, infection or injury, which requires careful interpretation of its values in conditions of concomitant comorbid background.

Pro-inflammatory cytokines, primarily interleukin-6 (IL-6) and IL-1b, as well as tumor necrosis factor alpha (TNF-alpha), are more directly involved in the pathogenesis of atherosclerosis and plaque destabilization. IL-6, produced by macrophages, adipocytes, and smooth muscle cells in the atheroma zone, is a key regulator of the transition from acute to chronic inflammation [22]. It stimulates the synthesis of CRP, fibrinogen, and also promotes endothelial activation and thrombosis. Elevated plasma IL-6 levels are associated with plaque instability, the severity of coronary atherosclerosis according to angiography, and an increased risk of death and reinfarction [23].

TNF-α, produced mainly by activated macrophages, enhances the expression of adhesion molecules, induces apoptosis of cardiomyocytes, and promotes the development of myocardial dysfunction [24]. Its elevated levels correlate with the severity of heart failure in the post-infarction period and independently predict mortality. However, the widespread clinical use of these cytokines is limited by the complexity and high cost of their determination, as well as high variability within a day.

Promising markers include soluble forms of adhesion molecules, sICAM–1 and sVCAM-1, which are released into the bloodstream upon activation of the endothelium. Their concentration reflects the degree of endothelial dysfunction, a key link in the initiation and progression of atherosclerosis [25]. Elevated levels of sICAM-1 and sVCAM-1 are detected in patients with ACS already in the first hours and are associated with multivessel damage, high platelet aggregation potential and an increased risk of recurrent ischemia. Unlike CRP, these markers are more specific for vascular inflammation, which makes them attractive for inclusion in expanded prognostic panels.

Fibrinogen, an acute phase protein, is involved not only in coagulation, but also in inflammation: it promotes platelet aggregation, increases blood viscosity, and stimulates smooth muscle cell migration [26]. Its levels increase in ACS and correlate with the risk of thrombotic complications and death. Nevertheless, like CRP, fibrinogen is susceptible to the influence of external factors (smoking, obesity, infections), which reduces its independent prognostic power.

Among the new biomarkers, calprotectin, a complex of S100A8/S100A9 proteins secreted by neutrophils and monocytes upon their activation, is of particular interest. It stimulates cytokine production, enhances leukocyte migration, and participates in plaque destabilization [27]. Studies show that the level of calprotectin increases in patients with ACS compared with chronic coronary heart disease and predicts the development of complications. Moreover, it remains in a stable form in plasma, which makes it promising for routine use.

Hemopexin, a protein that binds free heme, is also attracting attention as a marker of oxidative stress and inflammation. Hemolysis or massive myocardial necrosis releases heme, which has pro-oxidant and pro-inflammatory effects [28]. Hemopexin neutralizes it, but its own level decreases, which is associated with a more severe course of a heart attack and a worse prognosis. Thus, low hemopexin values may reflect not only the intensity of damage, but also the depletion of antioxidant protection.

In recent years, combined indices based on routine indicators of a general blood test have acquired particular predictive value, since they reflect the dynamic relationship between the pro- and anti-inflammatory components of the immune system.

The neutrophil-lymphocyte ratio (NLR), a simple, cheap and easily calculated indicator, demonstrates a high predictive ability [29]. A high NLR indicates activation of innate immunity (neutrophils) while suppressing adaptive immunity (lymphopenia), which is typical for severe systemic inflammation. Meta-analyses show that NLR > 5-6 is associated with an increased risk of death, reinfarction, and the need for repeated revascularization [30]. At the same time, its prognostic significance is not inferior to, and in some studies surpasses, traditional markers such as CRP.

The lymphocyte-monocyte ratio (LMR) reflects the balance between anti-inflammatory lymphocytes and pro-inflammatory monocytes. Reduced LMR is associated with higher inflammatory activity and worse outcomes.

The systemic immune-inflammatory index (SII), calculated using the formula: (platelets × neutrophils) / lymphocytes, integrates three key components – inflammation (neutrophils), immunosuppression (lymphocytes) and thrombogenicity (platelets). SII showed a high discriminatory ability in relation to both cardiac and allo-causal deaths, especially in patients with multivessel lesion.

Thus, biomarkers of inflammation represent a multilevel system for assessing the biological activity of the process in ACS. From simple and accessible (NLR, CRP) to complex molecular indicators (IL-6, calprotectin), they make it possible to refine the prognosis, identify high—risk patients, and potentially correct therapy. A promising direction is the creation of multicomponent prognostic models that combine clinical, laboratory, and imaging data with inflammatory indexes to build personalized patient management algorithms.

DISCUSSION.

An increase in the levels of inflammatory biomarkers in acute coronary syndrome is not an epiphenomenon or a secondary reaction to tissue damage; it reflects the activity of the pathological process at the systemic and local levels and closely correlates with the morphofunctional characteristics of coronary atherosclerosis, as well as with clinical outcomes. Long-term observational and interventional studies have convincingly demonstrated that the severity of the inflammatory response is directly related to the anatomical and functional volume of damage to the coronary bed.

Thus, in patients with high levels of C-reactive protein, IL-6, TNF-α and NLR, multivessel lesion was significantly more often detected upon admission according to coronary angiography. Such markers are associated with a greater extent of atherosclerotic plaques, more pronounced calcification and diffuse lesion, which complicates revascularization and increases the risk of perioperative complications [31]. In addition, increased inflammatory activity is often accompanied by the presence of plaques in other coronary arteries, which, although they did not cause an index event, show signs of instability (thin fibrous capsule, large lipid core, spontaneous hyperemia according to OCT or IVUS). This indicates the systemic nature of the process, when inflammation affects not one,

but all coronary vessels, increasing the likelihood of recurrent ischemic episodes.

Of particular importance is the relationship between biomarkers and atherosclerotic plaque instability. In vivo studies and postmortem analyses show that plaques prone to rupture or erosion are characterized by massive infiltration by macrophages, T lymphocytes, and neutrophils, and high expression of MMP-9, IL-1b, and sCD40L [32]. Accordingly, patients with ACS with elevated levels of these markers are more likely to suffer events caused by plaque rupture rather than thrombosis on the background of stable stenosis. This is confirmed by optical coherence tomography (OCT) data, where high NLR and CRP values are associated with signs of a vulnerable plaque: a thin fibrous capsule (<65 microns), a large area of the lipid core, and micro-thrombosis.

Clinically, this translates into an increased risk of recurrent myocardial infarction. Even with successful index artery revascularization, patients with a high inflammatory profile remain at increased risk. For example, the MACE (Major Adverse Cardiovascular Events) study showed that patients with NLR > 6 had a 2.3-fold higher risk of recurrent heart attack during the first year compared with patients with NLR < 3. Similar data were obtained for IL-6, CRP, and SII. It is assumed that chronic activation of the immune system contributes to the rapid progression of new or previously unstable plaques, as well as increases the thrombogenic activity of platelets and endothelium.

The association of inflammation with the development of acute and chronic heart failure is no less significant. After a myocardial infarction, the inflammatory cascade continues in the area of damage: M1 class macrophages promote the lysis of necrotic cells, but with excessive activity they enhance apoptosis of the surrounding myocardium and fibrosis. High levels of TNF-α, IL-1β, and IL-6 are associated with more pronounced postinfarction remodeling of the left ventricle – an increase in its terminal diastolic volume, a decrease in ejection fraction, and aneurysm formation. This is manifested in a higher frequency of hospitalizations for congestive heart failure in the next 6-12 months [33].

Of particular concern is the association of inflammatory markers with cardiac death, including sudden cardiac arrest and death from progressive heart failure. A meta-analysis of 27 studies (more than 15,000 patients) showed that elevated CRP increases the risk of cardiac death by 60-80%, and high NLR by more than 2 times. At the same time, these associations persist even after correction for ejection fraction, heart attack size, age, and concomitant diseases [34]. It is assumed that systemic inflammation contributes to the electrical instability of the myocardium due to impaired conduction, elongation of repolarization and the formation of arrhythmogenic substrates.

Thus, an increase in the level of inflammatory biomarkers in ACS is not just a laboratory finding, but a clinically significant sign of an aggressive course of the disease. It signals a large-scale lesion of the coronary bed, a high probability of unstable plaques, an increased risk of recurrent ischemic events, the development of myocardial dysfunction and, ultimately, an unsatisfactory long-term prognosis. These data substantiate the need to include inflammatory indicators in a comprehensive assessment of the patient and can serve as a basis for enhanced therapy, more thorough monitoring and early intervention.

Despite the fact that traditional risk factors for cardiovascular diseases such as hypertension, dyslipidemia, diabetes mellitus, smoking, obesity, and hereditary predisposition remain key elements of risk stratification in acute coronary syndrome, their prognostic ability in individual cases is often limited. Many patients with a "favorable" profile in these parameters suffer severe complications, while those with multiple risk factors may have a relatively benign course. In this context, additional markers reflecting the biological activity of the process are of particular importance, among which C-reactive protein (CRP) and neutrophil-lymphocyte ratio (NLR) have demonstrated convincing evidence of an independent prognostic contribution [35].

Many prospective cohort studies and post-hoc analyses of large registries (including PLATO, TRITON-TIMI 38, CLARITY-TIMI 28) have shown that elevated levels of CRP and NLR in the acute period of ACS are significantly associated with an increased risk of death, reinfarction, stroke, and the need for repeated revascularization. At the same time, the statistical significance of these associations remains even after multifactorial correction for age, gender, concomitant diseases, left ventricular ejection fraction, degree of coronary lesion, lipid profile and therapy [36].

These data indicate that CRP and NLR not only correlate with the severity of the disease, but also carry additional, independent prognostic information that cannot be extracted from traditional clinical and laboratory parameters. It is assumed that they reflect latent biological variability – the intensity of systemic inflammation, the degree of immune activation, thrombogenic activity, and the general "aggressiveness" of the atherosclerotic process — which makes them valuable tools for clarifying risk in patients with the same clinical picture but different biological backgrounds.

However, despite convincing evidence of their prognostic value, the widespread introduction of CRP, NLR and other inflammatory markers into routine clinical practice faces a number of significant limitations that require a systemic solution.

First, the lack of standardization of determination methods creates serious barriers to comparability of results between laboratories and research. The level of CRP can be measured using various immunoanalytical techniques (latex agglutination, immunonephelometry, ELISA), each of which has its own sensitivity, linearity range, and detection threshold [37]. The difference between standard and highly sensitive CRP (hs-CRP) is particularly critical, the latter of which allows detecting low concentrations (0.3–10 mg/l) and more accurately assessing cardiovascular risk in asymptomatic individuals. At the same time, a number of medical institutions still use a non-selective definition, which reduces the informative value of the data.

Secondly, the problem of establishing unified thresholds remains unresolved. Although a threshold of 5 or 6 is often used for NLR, different studies suggest different "optimal" values – from 3.5 to 8, depending on the population, the method of analysis (ROC curve, Youden Index) and the observed outcome (mortality, reinfarction, heart failure). This makes it difficult to interpret the results in daily practice and reduces the reproducibility of clinical decisions. A similar situation is observed with CRP: the 3 mg/L limit recommended by the AHA/CDC is not always applicable to patients with ACS, whose levels may exceed 10 mg/l on the first day.

Thirdly, validation of biomarkers in different populations is necessary. Most of the data were obtained in cohorts of European and North American countries, while other thresholds, marker dynamics, and their prognostic significance may be observed in Asian, African, and Latin American populations. For example, in patients with chronic infections (hepatitis, HIV), autoimmune diseases, or renal insufficiency, CRP and NLR levels may be chronically elevated, which distorts their interpretation in the context of ACS [38]. In addition, age, gender, ethnicity, and concomitant therapy (for example, statins, which themselves reduce CRP) have a modulating effect on inflammatory markers, which must be taken into account when building prognostic models.

Thus, although CRP and NLR can already be considered as independent predictors of adverse outcomes in ACS, their clinical implementation requires addressing key methodological issues. Only if laboratory techniques are standardized, population-based reference intervals are established, and large multicenter studies are conducted in diverse groups of patients, these markers can be integrated into official clinical guidelines and widely used for personalized risk assessment.

The integration of inflammatory markers into existing prognostic models, such as the GRACE scale (Global Registry of Acute Coronary Events) and TIMI risk assessment (Thrombolysis in Myocardial Infarction), is one of the most promising areas in modern cardiology aimed at improving the accuracy of stratification of patients with acute coronary syndrome. These scales, based on clinical, electrocardiographic, and laboratory parameters (age, blood pressure, heart rate, creatinine concentration, signs of stagnation, cardiogenic shock, ST elevation, and increased troponins), have already proven effective in assessing the short- and medium-term risk of death and serious cardiovascular events. However, their discriminatory ability, measured by the area under the curve (AUC), in most cases ranges from 0.70–0.80, which leaves room for improvement, especially in patients with intermediate risk, where clinical decisions are often uncertain.

The addition of inflammatory biomarkers such as C-reactive protein (CRP), neutrophil-lymphocyte ratio (NLR), or systemic immune-inflammatory index (SII) to these models increases their prognostic informative value. Studies show that the inclusion of such indicators in the GRACE scale leads to an increase in AUC by 0.05–0.12, which is statistically and clinically significant. Moreover, an analysis of the improvement in risk reassessment (IRR) demonstrates that the addition of inflammatory markers makes it possible to correctly redistribute up to 15-25% of patients from the intermediate risk group to high or low risk categories, which directly affects the choice of management tactics: intensification of therapy, an early invasive strategy, or, conversely, a more conservative approach[39]. For example, a patient with a moderate GRACE score but high NLR and CRP may be transferred to a high-risk group, which justifies performing coronary angiography in the first 24 hours and prescribing more aggressive drug therapy.

However, the true potential for improving the accuracy of prognosis is revealed when switching from single markers to multifactorial biomarker panels combining data on inflammation, coagulation, oxidative stress, and myocardial remodeling [40]. Such panels may include, for example, IL-6, TNF-α, sICAM-1, hemopexin, calprotectin, as well as markers of myocardial damage (high sensitivity troponins, GFAP), endothelial function (adiponectin, endothelin-1) and thrombosis (D-dimer, fibrinogen). A joint analysis of these indicators allows us to build a comprehensive "molecular map" of the patient's condition, reflecting not only the anatomical lesion, but also the biological activity of the process. Similar approaches are already being tested in research projects such as PROSPECT, IBIS, and GLOBAL LEADERS, where biomarker profiles are combined with intravascular imaging data (IVUS, OCT) [41].

The integration of biomarkers with visualization data offers a special perspective. For example, the combination of high NLR with signs of a thin fibrous capsule according to optical coherence tomography (OCT) or a large volume of uncalcified plaque according to IVUS makes it possible to accurately identify patients with a systemic inflammatory background and local instability who require special attention. Such patients

may be candidates for extended therapy, including intensive anti-inflammatory treatment (e.g., colchicine) or closer monitoring on an outpatient basis.

An even deeper level of personalization is achieved when genetic profiling is enabled. Polymorphisms of genes involved in the regulation of inflammation (for example, IL6, TNF-α, CRP, NLRP3) can determine an individual's predisposition to excessive immune activation and, consequently, to the aggressive course of ACS [42]. Patients with certain haplotypes may exhibit higher levels of CRP and IL-6 with the same degree of myocardial damage, which makes them potential candidates for targeted anti-inflammatory therapy. There is already evidence that the effectiveness of canakinumab in the CANTOS study was higher in patients with an initial increase in IL-6, which indicates the possibility of biomarker-oriented selection for specific treatment strategies [43].

It can be concluded that the future of prediction in ACS lies not in the use of separate "universal" scales, but in the creation of dynamic, adaptive models combining clinical parameters, laboratory markers, imaging data and genetic information. Such algorithms will allow not only to accurately assess the risk, but also to predict the response to therapy, determine the optimal intensity of intervention and create individualized monitoring plans. The implementation of these approaches requires multidisciplinary collaboration, standardization of techniques, the creation of biobanks and the development of AI tools for processing multidimensional data. Nevertheless, the first steps have already been taken, and in the coming years we can expect a transition from the "average patient" to personalized cardiology, where the prognosis and treatment are determined not only by the anatomy, but also by the biology of the disease.

CONCLUSIONS.

The analysis of modern data indicates the central role of systemic inflammation in the pathogenesis of acute coronary syndrome, which goes beyond the traditional concepts of atherosclerosis as a passive deposition of lipids. Inflammatory processes are involved at all stages, from initial endothelial dysfunction and atherosclerotic plaque formation to its destabilization, rupture, and subsequent postinfarction myocardial remodeling. In this context, biomarkers of inflammation acquire not only pathophysiological, but also clinically significant prognostic value, making it possible to identify patients with a high risk of adverse cardiovascular events in the early stages of the disease.

It has been shown that an increase in the levels of both traditional (C-reactive protein, IL-6, TNF-α) and new markers (calprotectin, hemopexin, sICAM-1) is associated with more pronounced coronary lesion, instability of atherosclerotic plaques, an increase in the area of infarction and an increased incidence of complications. Combined indices based on the parameters of a general blood test demonstrate a special prognostic value, primarily the neutrophil-lymphocyte ratio (NLR), lymphocyte-monocyte ratio (LMR) and the systemic immune-inflammatory index (SII). These indicators, despite their simplicity of calculation and accessibility, reflect a complex balance between the pro- and anti-inflammatory mechanisms of the immune system and demonstrate high predictive ability in real clinical practice.

The independent prognostic contribution of CRP and NLR has been convincingly proven, which persists even after correction for age, concomitant diseases, left ventricular function, and traditional risk factors. This confirms their potential as additional risk stratification tools that can improve discrimination against patients with intermediate risk according to the GRACE and TIMI scales. The integration of inflammatory markers into existing prognostic models increases their informativeness, as evidenced by an increase in the area under the ROC curve (AUC) and positive values of the risk reassessment improvement indicator (NRI).

At the same time, the widespread introduction of biomarkers into routine clinical practice is hindered by a number of methodological and organizational barriers. The lack of uniform definition standards, differences in sensitivity of techniques (for example, between standard and highly sensitive CRP), the lack of unified thresholds, and insufficient validation in diverse populations (including patients with concomitant chronic diseases, different ethnicities, and age groups) limit their interpretability and comparabilityAt the same time, the widespread introduction of biomarkers into routine clinical practice is hindered by a number of methodological and organizational barriers. The lack of uniform definition standards, differences in sensitivity of techniques (for example, between standard and highly sensitive CRP), the lack of unified thresholds, and insufficient validation in diverse populations (including patients with concomitant chronic diseases, different ethnicities, and age groups) limit their interpretability and comparability. In this regard, large-scale multicenter studies are needed to standardize laboratory protocols and establish population-based reference intervals.

A promising direction is the transition from the assessment of individual markers to multifactorial biomarker panels that combine data on inflammation, coagulation, oxidative stress, and vascular wall remodeling. Even higher prediction accuracy can be achieved by integrating biomarkers with instrumental imagA promising direction is the transition from the assessment of individual markers to multifactorial biomarker panels that combine data on inflammation, coagulation, oxidative stress, and vascular wall remodeling. Even higher prediction accuracy can be achieved by integrating biomarkers with instrumental imaging data (OCT, IVUS, CT angiography), which allows combining anatomical assessment of the coronary

bed with the biological activity of the process. Further deepening of the personification of the prognosis is possible with the inclusion of genetic markers of predisposition to inflammation, which opens the way to targeted therapy.

Accordingly, biomarkers of inflammation are not just laboratory indicators, but a reflection of the biological essence of the disease, which can transform the approach to the prediction and treatment of ACS. Their rational use can facilitate the transition from universAccordingly, biomarkers of inflammation are not just laboratory indicators, but a reflection of the biological essence of the disease, which can transform the approach to the prediction and treatment of ACS. Their rational use can facilitate the transition from universal algorithms to personal

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