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RESEARCH ARTICLE

MODERN APPROACHES TO EARLY DIAGNOSIS OF CORONARY HEART DISEASE IN PATIENTS WITH METABOLIC SYNDROME

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Abstract: The aim of the work is to systematize modern evidence-based approaches to early detection of coronary heart disease (CHD) in patients with metabolic syndrome, characterized by high atherothrombotic vulnerability and heterogeneity of phenotypes. The article discusses updated clinical diagnostic pathways based on European and North American recommendations, the role of disease probability stratification, the use of coronary calcium scoring, coronary CT angiography, functional stress tests, and positron emission tomography with quantitative assessment of myocardial blood flow to detect both obstructive and microcirculatory ischemia.The article discusses promising biomarkers of inflammation and lipid metabolism, including the hs-CRP/HDL-C ratio, and the integration of imaging and laboratory data into personalized screening algorithms.The authors conclude that a multi-level early diagnosis model that combines clinical and biochemical indicators and step-by-step imaging is appropriate, with calcium scoring and the assessment of the likelihood of coronary artery disease playing a key role in the initial selection of patients with MS, and quantitative PET perfusion being used for suspected microvascular forms. The main points are consistent with the ESC 2024 guidelines on chronic coronary syndromes and the ACC/AHA guidelines for the management of patients with chest pain.

Keywords: Coronary artery disease, metabolic syndrome, early diagnosis, coronary calcium scoring, CT angiography, positron emission tomography, hs-CRP, microcirculatory dysfunction.

INTRODUCTION

Metabolic syndrome is a cluster of interrelated disorders of carbohydrate and lipid metabolism, visceral obesity, arterial hypertension and chronic low-level inflammation, forming conditions for accelerated development of the atherosclerotic process and functional disorganization of the coronary bed. At the population level, it is associated with an advanced accumulation of cardiovascular risk factors and early onset of coronary heart disease, as well as with a steady trend towards an increase in the relative contribution of non-obstructive and diffuse forms of ischemia.

The clinical significance of the problem is determined not only by the high prevalence of the syndrome in working-age groups, but also by the fact that traditional algorithms for diagnosing IHD, which focus on identifying a hemodynamically significant stenotic plaque, are not sufficiently sensitive to the microvascular and endothelial mechanisms of ischemia that are characteristic of some patients with a metabolic phenotype. As a result, there are diagnostic gaps in the early stages of the disease, when lifestyle interventions and pharmacotherapy are most effective for prevention.

The pathogenic axis "insulin resistance — subclinical inflammation — endothelial dysfunction" determines the features of the morphogenesis of coronary atherosclerosis in metabolic syndrome. Against the background of visceral obesity and metabolic imbalance, the production of pro-inflammatory mediators increases and oxidative stress is activated, which reduces the bioavailability of nitric oxide, disrupts the vasodilatory response, and increases thrombogenicity. In the coronary arteries, diffuse intimal infiltration increases, including the formation of low-density atheromas, which do not always cause critical narrowing of the lumen but are associated with plaque vulnerability and the risk of events.

In parallel, microcirculation is affected: remodeling of resistive vessels and deregulation of autoregulation lead to a decrease in coronary blood flow reserve, and the ischemic cascade is triggered at a lower load than in individuals without metabolic disorders. This dual nature of anatomical and functional mechanisms explains why patients with metabolic syndrome often experience a discrepancy between the severity of symptoms and the results of structural tests, as well as variability in standard exercise tests.

In recent years, there has been a shift in cardiac practice from a purely stenosis-centric paradigm to a broader concept of chronic coronary syndromes, which includes a spectrum of conditions with anatomically non-obstructive arteries and functional microcirculatory disorders. For the cohort with metabolic syndrome, this evolution is particularly significant, as it allows for the formalization of diagnostic pathways for patients with typical or equivalent symptoms of ischemia in the absence of significant stenoses based on coronary CT angiography.

Against this background, the role of methods capable of recording subclinical markers of atherosclerotic load and early functional deviations is increasing. Such markers include coronary artery calcification as an integral trace of long-term exposure to risk factors, quantitative parameters of myocardial blood flow according to positron emission tomography, as well as inflammatory-lipid composites reflecting the current activity of atherogenesis. Their use in stratified algorithmizing allows for more accurate selection of patients for advanced imaging and early initiation of cardioprotective therapy.

The practical challenge of early diagnosis in this category of patients is to strike a balance between minimizing missed ischemia and preventing excessive, resource-intensive interventions. On the one hand, relying solely on clinical assessment of the likelihood of coronary artery disease and classic stress tests may lead to underestimation of microvascular forms and diffuse ischemia, which are characteristic of the metabolic phenotype. On the other hand, the indiscriminate use of high-tech imaging methods is associated with resource overspending and the risk of diagnostic findings that do not change the treatment approach.

Under these conditions, a multi-level route appears to be rational, including a preliminary assessment of the probability of the disease, taking into account gender, age, symptoms, and a combination of risk factors, the early use of low-dose and reproducible surrogate indicators of atherosclerosis, and, in the presence of a clinical and anatomical discrepancy, functional verification of ischemia using methods with a quantitative assessment of perfusion. This approach does not replace, but rather complements, traditional diagnostic tools, reallocating them according to the stages and tasks.

The scientific and practical relevance of the topic is enhanced by epidemiological trends, including an increase in the prevalence of obesity and carbohydrate metabolism disorders, as well as the aging of the patient population, where polymorbidity makes classical diagnostic schemes less specific. An additional dimension is the gender-specific nature of the manifestations: microcirculatory dysfunction is more common in women with metabolic syndrome, which requires targeted functional verification in the absence of positive anatomical test results. The prospect of personalized prevention is also important: early detection of subclinical coronary pathology allows for timely intensification of therapy focused on lipid profile, inflammatory activity, and vascular function, as well as more strict control of glycemic parameters, blood pressure, and body weight.

This study aims to systematize modern approaches to the early diagnosis of coronary artery disease in patients with metabolic syndrome, highlighting the role of calcium scoring as a primary stratification filter that clarifies the value of coronary CT angiography in patients with intermediate disease probability, as well as the significance of functional methods, including positron emission tomography with quantitative assessment of myocardial blood flow and reserve, for the recognition of microcirculatory forms of ischemia. Additionally, the role of laboratory indicators of low-level inflammation and lipid imbalance in early selection algorithms for visualization is being considered.

The working hypothesis is that the integration of clinical probability with early surrogates of atherosclerotic burden and quantitative perfusion imaging provides the best combination of diagnostic accuracy, prognostic utility, and cost-effectiveness for patients with metabolic syndrome. To verify this hypothesis, we will compare diagnostic trajectories based on their ability to detect clinically significant ischemia at preclinical stages, influence treatment choices, and predict adverse outcomes in the medium term.

Materials and methods of research.

The review was based on an analysis of the current clinical guidelines of the European Society of Cardiology for chronic coronary syndromes (2024 edition) and The Emergency Rescue Service guidelines for assessing patients with chest pain, as well as studies on the prognostic value of coronary calcium scoring and modern methods of functional imaging.

Included data on quantification of myocardial blood flow by PET, as well as studies on systemic markers of low-level inflammation and composite indices reflecting the interaction of inflammatory and lipid pathways in MS (metabolic syndrome).

The search strategy covered sources from recent years, with a focus on updated guidelines and large cohort studies.

Results and discussions.

The modern doctrine of early diagnosis of CHD in patients with MS involves a sequential risk stratification, in which the primary decision points are the clinical probability of the disease and the measured surrogates of the atherosclerotic load. According to ESC 2024, assessing the probability of CHD and then selecting a test allows to minimize overdiagnosis and direct resource methods to the groups with the greatest expected benefit.

Within this approach, Agatston's coronary artery calcium scoring is recognized as a highly informative tool for early preclinical stratification: zero calcification is associated with an extremely low immediate probability of events, while an increase in the index correlates with long-term risk in both the general middle-aged population and individuals with carbohydrate metabolism disorders. For patients with MS who have accelerated calcification, the inclusion of calcium scoring at an early stage allows for the identification of hidden atherosclerotic burden and the refinement of subsequent imaging strategies [4].

Coronary CT angiography, being a method with a high negative predictive value, is recommended for intermediate probability of CHD and suspicion of an anatomical substrate of ischemia. In this cohort, MS is often associated with diffuse non-stenotic lesion and remodeling, where CT angiography allows to identify unfavorable plaque phenotypes and assess the overall atherosclerotic burden, with subsequent intensification of preventive therapy. When the symptomatology indicates ischemia with moderate or uncertain probability, functional tests remain an alternative; The choice between stress-ECG, MRI-stress perfusion, and scintigraphy is determined by availability and clinical context. Updated guidelines for the management of chest pain emphasize the importance of an informed choice of the first test and the value of CT angiography in patients without a high likelihood of acute coronary syndrome [1].

For MS phenotypes with a predominance of microcirculatory dysfunction and endothelial failure, especially in women and in individuals with a combination of insulin resistance and inflammatory markers, objective confirmation of reduced coronary blood flow reserve becomes crucial. Quantitative PET perfusion with calculation of hyperemic myocardial blood flow and reserve (MFR) has been standardized by expert documents and has shown high diagnostic and prognostic significance; A decrease in MFR reflects an unfavorable microvascular phenotype and is associated with an increased risk of events, regardless of the presence of obstructive stenoses. In ANOCA/INOCA scenarios, which are officially highlighted in the ESC update, the use of quantitative PET allows for early confirmation of ischemia and selection of patients for targeted therapy of vascular and metabolic disorders [6].

Laboratory indicators of low-level inflammation and lipid imbalance in patients with MS enhance the discriminatory capacity of clinical models. In particular, the hs-CRP/HDL-C ratio has demonstrated a link to long-term mortality and cardiovascular risk in population-based cohort analyses and within the framework of the cardio-reno-metabolic continuum (CRM syndrome), suggesting that this composite can be considered an accessible and standardized measure of systemic inflammation that contributes to atherogenesis. The inclusion of this relationship in the basic risk models improved their calibration and reevaluation of events, which opens up prospects for its application in the primary screening of patients with MS. However, the interpretation should be based on the association with apoB, Lp(a), and glycemic parameters, as well as imaging signs of subclinical atherosclerosis [9].

From the perspective of public health, it is rational to start the implementation of a step-by-step algorithm for early diagnosis in patients with MS with a clinical assessment of the likelihood of CHD, followed by the use of calcium scoring as a low-dose, fast, and reproducible test that improves the accuracy of stratification. In asymptomatic individuals with a zero-calcium score and no concerning clinical signs, risk factor modification and dynamic monitoring remain the priority [5].

When moderate or high calcification is detected, it is reasonable to proceed to CT angiography to clarify the anatomy of the lesion. If there is a discrepancy between symptoms and anatomy, or if microvascular ischemia is suspected, functional imaging with quantitative assessment of blood flow is advisable, where PET has the highest level of validation. This strategy is in line with the key points of the ESC 2024 and the recommendations for the management of patients with chest pain..

Table 1. Comparison of key methods for early diagnosis of CHD in patients with metabolic syndrome

Method	Primary diagnostic purpose	Clinical situations of preferred use	Validated predictive value
Coronary Calcium Score (Agatston)	Quantification of subclinical atherosclerotic load	Asymptomatic or mildly symptomatic patients with MS during initial risk stratification	Associated with long-term mortality and events; improves risk discrimination, including cohorts with carbohydrate metabolism disorders
Coronary CT	Identification of	Intermediate pre-test	High negative predictive value;

angiography	the anatomical substrate of ischemia and adverse plaque phenotypes	probability; discrepancy between clinic and biomarkers; therapy planning	improved diagnostics in the early stages of the route
Functional stress tests (Echocardiography, MRI, SPECT)	Confirmation of ischemia-induced load	Symptomatic patients with intermediate probability; clarification of the significance of stenoses	Proven predictive role; choice depends on availability and context
PET with MBF/MFR quantification	Detection of microcirculatory dysfunction and diffuse ischemia	Suspicion of ANOCA/INOCA; discrepancy between symptoms and anatomy; MS phenotypes with endothelial dysfunction	Standardized criteria; MFR predicts events independently of stenoses

Comparison of the methods demonstrates different diagnostic optics and time horizon of prognostic relevance, which is especially important for a heterogeneous cohort of patients with metabolic syndrome. Coronary calcium scoring acts as an indicator of accumulated atherosclerotic load and allows for early division of patients into trajectories for further examination; the clinical value here is determined by the high negative prognostic significance of the zero index and the dose-dependent increase in long-term risk with an increase in the Agatston score [2].

Coronary CT angiography expands the assessment from quantitative burden to qualitative characterization of plaque morphology, which is especially critical in diffuse and non-stenotic processes typical of metabolic phenotypes, where anatomical signs of vulnerability precede functional decompensation. Functional stress tests provide evidence of induced ischemia and allow for the separation of hemodynamically significant stenoses from incidental findings, but their interpretation in patients with MS is complicated by the frequent presence of microcirculatory dysfunction and heterogeneous vascular reactivity, which can lead to false-negative or ambivalent results in the presence of moderate diffuse ischemia [8].

PET with quantitative assessment of myocardial blood flow and reserve fills this gap by detecting abnormalities at the microvascular level and providing a personalized approach focused on vascular and metabolic targets, even in the absence of significant epicardial obstruction.

Taken together, the comparative analysis confirms the need for an adaptive rather than a linear diagnostic strategy: starting with an accessible and standardized calcium scoring, moving to anatomical imaging when significant calcification is present, and incorporating quantitative perfusion assessment when there is a discrepancy between clinical and anatomical findings or when there are signs of endothelial and microcirculatory dysfunction.

Table 2. A set of indicators for early selection of patients with MS for advanced imaging

Indicator	Thresholds and Interpretation	Practical significance in MS
Coronary Calcium Index (Agatston)	0 — extremely low immediate probability of events; 1–99 — low-moderate risk; ≥100 — significant atherosclerotic load with increased long-term risk; ≥400 — high risk; specific tactics depend on age and clinic	A quick stratification filter for CT angiography and prevention intensification
hs-CRP/HDL-C ratio	An increase in the indicator is associated with an increase in long-term mortality and the risk of CVD events; integration improves the predictive ability of models	Reflects the interaction between inflammation and dyslipidemia; an available laboratory metric for early vulnerability
Quantitative coronary blood flow (MBF) and reserve (MFR) by PET	A decrease in hyperemic MBF and/or MFR indicates coronary microvascular dysfunction	Confirmation of ischemia in non-obstructive anatomy; risk stratification and targeting of therapy

The composites and quantitative parameters presented in the second table form a bridge between routine stratification and high-tech imaging. The coronary calcium index, as an integrator of long-term exposure to risk factors, reflects the accelerated pace of vascular aging in the context of MS and serves as a threshold filter for selection for CT angiography; At the same time, the interpretation should take into account age, gender, and the clinical picture, in order to avoid both overdiagnosis in young patients with a low probability and missing a significant process in older patients with a mild course.

The hs-CRP/HDL-C ratio adds a dynamic component to stratification, capturing the degree of systemic inflammation in the context of an atherogenic lipid profile. An increase in this ratio in patients with normal or moderate calcification levels indicates an active phase of atherogenesis and increases the a priori likelihood of hidden ischemia, thereby rationalizing the need for advanced imaging. Quantitative indicators of myocardial blood flow and coronary reserve on PET close the diagnostic lacuna in patients with a mismatch between symptoms and anatomy, objectifying the microvascular phenotype, which in the MS cohort is associated with insulin resistance, endothelial dysfunction, and slowly progressive diffuse ischemia [10].

This three-tiered indicator system provides a coherent early selection process: the laboratory and calcification "sieve" generates a well-founded request for imaging, while quantitative perfusion clarifies the pathophysiological mechanism of ischemia and provides a prognosis, allowing for the synchronization of pharmacotherapy intensity with the biological activity of the disease.

In addition, it should be noted that patients with MS are more likely to have CHD phenotypes that are not limited to critical stenoses of the epicardial arteries. The ESC update emphasizes the need to identify the causes of ischemia and stratify patients with ANOCA/INOCA, including through tests for endothelial reactivity and assessment of coronary reserve. This paradigm shift reduces the risk of under-examination of patients with severe symptoms and "clean" anatomy according to CT scans, which is especially common in women and patients with severe insulin resistance [7].

The integration of international recommendations with national practice involves adapting the routes to take into account the availability of technologies and epidemiology. Russian clinical resources and professional publications consistently emphasize the role of calcium scoring as a screening technique at early stages, as well as the need to expand the set of diagnostic tools to cover microcirculatory phenotypes. This is consistent with the observed trend of increasing the use of cardiac CT and cardiac screening programs in high-risk patients.

CONCLUSION

Early diagnosis of coronary heart disease in patients with metabolic syndrome is most effective when clinical assessment is integrated with multilevel imaging and informative biomarkers of the inflammatory-lipid continuum.

Coronary calcium scoring should be considered as a primary stratification tool that can identify patients with subclinical atherosclerotic burden, requiring anatomical clarification and intensified prevention, with low radiation exposure and high reproducibility.

Coronary CT angiography at the intermediate probability stage allows for the detection of unfavorable plaque phenotypes and diffuse lesions characteristic of MS, thereby preventing underestimation of risk in the absence of critical stenoses. Functional stress tests remain relevant for confirming induced ischemia, but in patients with a predominance of the microcirculatory mechanism, they should be supplemented by quantitative methods of perfusion assessment.

Positron emission tomography with calculation of myocardial blood flow and coronary reserve provides verification of microcirculatory dysfunction and strengthens the prognostic model, especially in scenarios of clinical and anatomical discrepancy.

Inclusion of the hs-CRP/HDL-C ratio in the set of early indicators increases the accuracy of selection for in-depth imaging by fixing the active inflammatory phase of atherogenesis, which is of particular value in moderate calcification and diffuse atherosclerosis.

The combination of these arguments confirms the advantages of an adaptive approach, in which the diagnostic trajectory is determined not by a single test, but by a consistent interpretation of clinical, laboratory, and imaging data. This approach reduces the risk of both missed ischemia and unnecessary interventions, while ensuring timely initiation of cardioprotective therapy in patients with metabolic syndrome.

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