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INFLAMMATION INDICATORS AND LEPTIN LEVEL IN PATIENTS WITH ISCHEMIC HEART DISEASE

Ukazovatele zápalu a koncentrácia leptínu u pacientov s ischemickou chorobou srdca

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SUMMARY

Background: The pathogenic bases of destabilizing the flow of ischemic heart disease are not studies well enough.

Aim: to study the plasma concentration and interrelation of inflammation biomarkers of C-reactive protein, tumor-necrotic factor-α and leptin level in patients with ischemic heart disease of different nature of flow and to define their diagnostic value as of indicators for destabilizing the atherosclerotic process.

Patients and methods: 86 male patients with ischemic heart disease of the average age of 56.2±5.1 have been examined. 29 patients showed stable ischemic heart disease of functional class II, 31 patients - ischemic heart disease of functional class III, while 26 patients were diagnosed with unstable ischemic heart disease. The control group included 26 practically healthy men of matching age who volunteered to participate. All the patients were examined according to the Guidelines of the European Society of Cardiologists (ESC, 2013). The plasma concentrations of highly sensitive X-reactive protein, tumor--necrotic factor-α and leptin were determined by immune-enzyme methods. The statistical analysis was made with the help of software kits Microsoft Excel, Statistica for Windows 6.0.

Results: the patients with ischemic heart disease the levels of the studied indices tended to grow and were higher in comparison with reference values, the most visible changes being detected in patients with unstable angina. The destabilized process showed the valid increase of the levels of highly sensitive C-reactive protein and tumor-necrotic factor-α in 92.3 % and 100% patients, leptin level - in 84.6 % patients correspondingly. The critical limit values allowing to suggest the activation of latent inflammation irrespective of presence or absence of clinical symptoms were identified. To them refer the levels of plasmatic highly sensitive C-reactive protein - 2.57 mg/ml, tumor-necrotic factor-α - 2.44 pg/ml, leptin - 18.44 ng/mL. The information value and capability of destabilization model of ischemic heart disease significantly rose at simultaneous use of such two markers of non-specific inflammation as C-reactive protein and tumor-necrotic factor-α. Adding leptin to the mathematic model did not show any significant impact on its information capacity.

Conclusions: identifying combinations of levels of highly sensitive C-reactive protein >2.97 mg/L and tumor-necrotic factor-α >2.44 pg/ml possesses maximal prognostic capacity with regard to atherosclerosis destabilization and development of cardiovascular complications in patients with stable ischemic heart disease.

Key words: ischemic heart disease, atherosclerosis, C-reactive protein, tumor-necrotic factor-α, leptin.

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SÚHRN

Východisko: Patogénne základy destabilizujece tok pri ischemickej chorobe srdca nie sú dosť dobre známe.

Cieľ práce: študovať plazmatické koncentrácie a vzájomné vzťahy medzi biomarkermi zápalu – C-reaktívnym proteínom, faktorom-alfa nekrotizujúcim tumory a koncentráciou leptínu u pacientov s ischemickou chorobou srdca rôznej povahy a definovať ich diagnostickú hodnotu ako ukazovateľov destabilizácie aterosklerotického procesu.

Súbor a metódy: Autori vyšetrovali 86 mužských pacientov s ischemickou chorobu srdca priemerného veku 56,2 ± 5,1 rokov. Dvadsaťdeväť pacientov malo stabilnú ischemickú chorobou srdca funkčnej triedy II; 31 pacientov ischemickú chorobu srdca funkčnej triedy III, pričom 26 pacientov bolo diagnostikovaných s nestabilnou angínou pectoris. Kontrolná skupina zahŕňala 26 dobrovoľníkov, prakticky zdravých mužov zodpovedajúcich veku. Všetci pacienti boli vyšetrení v súlade s pokynmi Európskej kardiologickej spoločnosti (European Society of Cardiology ESC, 2013). Plazmatické koncentrácie vysoko citlivého C-reaktívneho proteínu, nekrotického faktor--α nádorov a leptínu boli stanovené imunnoenzýmovými metódami. Štatistická analýza sa urobila pomocou softvérových balíkov Microsoft Excel, Statistica pre Windows 6.0.

Výsledky: Pacienti s ischemickou chorobou srdca mali tendenciu rastu študovaných indexov a boli vyššie v porovnaní s referenčnými hodnotami, najviac viditeľné zmeny boli u pacientov s nestabilnou anginou pectoris. Destabilizovaný proces zistil zvýšenie koncentrácie vysoko citlivého C-reaktívneho proteínu a nekrotického faktor-α nádorov u 92,3 % a 100 % pacientov, koncentrácie leptínu u 84,6 % pacientov. Kritické limity umožňujú diagnostikovať aktiváciu latentného zápalu bez ohľadu na prítomnosť alebo neprítomnosť klinických príznakov. Odkazujú na ne koncentrácie vysoko citlivého C-reaktívneho proteínu v plazme – 2,57 mg/ml, nekrotického faktora-α nádorov – 2,44 pg/ml, leptínu – 18,44 ng/ml. Hodnota informácie a schopnosť destabilizácie modelu ischemickej choroby srdca výrazne vzrástla pri súčasnom použití týchto dvoch markerov nešpecifického zápalu – C-reaktívneho proteínu a nekrotického faktor--α nádorov. Pridanie leptín do matematického modelu neukázala žiadny významný vplyv na jeho informačnú hodnotu.

Záver: Kombinácia koncentrácie vysoko citlivého C-reaktívneho proteínu > 2,97 mg/l a nekrotického faktora-α tumorov > 2,44 pg/ml má maximálnu prognostickú schopnosť s ohľadom na aterosklerózy destabilizácii a vývoja kardiovaskulárnych komplikácií u pacientov so stabilnou ischemickou chorobou srdca.

Kľúčové slová: ischemická choroba srdca, ateroskleróza, C-reaktívny proteín, nekrotický faktor-α tumorov (TNF-α), leptín.

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The increase of incidence and 'juvenation' of ischemic heart disease (IHD), whose disease-causing factor is atherosclerosis, determines the necessity of active analysis of its occurrence and exploitation of effective preventive measures. Nowadays there exist a number of theories of pathogenesis of atherosclerosis, but still none of them has been able to reveal the disease processes and determine the importance of all risk factors to the full extent.

The researches of the last years confirmed that both the systemic latent inflammatory process and the local inflammation of coronary artery wall play an important role in atherosclerosis progressing and plaque instability. The tendency to rapid growth, the presence of immune inflammation, the increased activity of tissue enzymes in the area of a recent plaque, slight structure-forming processes, including calcinosis explain the susceptibility to forming micro-ruptures on the surface of a recent atheroma with the further development of atherothrombosis (9, 22).

With the aim of detecting immune inflammation, The European Society of Cardiology recommends to determine the level of fibrinogen and high-sensitivity C-reactive protein (hs-CRP) in serum/plasma blood of people with stable IHD (17). The results of several population researches contributed to the formation of the idea of C-reactive protein (CRP) as of self-consistent risk factor, an independent predictor of ischemic events in diverse vascular systems (coronary, cerebral, peripheral) as of both healthy people and patients with recorded atherosclerosis-related cardiovascular system diseases. In JUPITER research (members of the Justification for the Use of Statins in Preventions: an Intervention Trial Evaluating Rosuvastatin) the role of CRP, as of a self--consistent risk factor of IHD and of an interference subject related to the increased risk of atherosclerotic and cardiovascular failures in people without pre-existing cardiovascular (CV) disease and low or regular cholesterol level in low density lipoproteins (LDL), but with the increased content of CRP (> 2 mg/l) is proved (4). However, diagnostic limits of hs-CRP in blood plasma for predicting the risks of IHD are within regular level for general population (1 – 3 mg/l), evoking constant arguments about the reasonability of its identification. It is known, that this indicator becomes uninformative for stratification of CV risks if the concentration of hs-CRP is above 10 mg/l (25).

Atherosclerosis discussed from the point of view of chronical pathology of arterial wall, assumes the involvement of diverse immune inflammatory mechanisms into the pathological process, in which cytokines play the leading role as the mediums of intercellular cooperation. (11, 15, 23, 26). In clinical medicine it is common to determine the concentration of one of the cytokines – a tumor necrotic factor-α (TNF-α) as a reliable marker of inflammatory process. TNF-α has a pro-inflammatory effect, involving the induction of synthesis of other cytokines by endothelium, stimulating collagen production, increasing the expression of adhesion molecule and pro-coagulation activity (7). As we know, the level of TNF-α is higher in atherosclerotic plaques than in not affected vascular wall, and is much higher in plaques that are inflammatory active (2, 8). The increased level of TNF-α has a cardiotoxic effect, causes abiotic polymerization of acute inflammatory phase, stimulates proliferation of smooth muscle cells, and the activation of its receptors inducts necrocytosis through apoptosis (6, 12, 18). It is determined that TNF-α level increases with the presence of atherosclerosis, acute myocardial infarction (AMI) and chronic heart failure (CHF) (1).

Obesity is one of the proved factors of CV risk. As hormonal activity of fat tissue was revealed, the active study of complex interrelation between obesity, insulin resistance, leptin resistance, violation of lipid metabolism and atherosclerosis began. The referred data about the contribution of leptin secreted by the fat tissue to the atherogenesis are rather contradictory.

Some studies refer to the correlation of leptin and development of insulin-resistance and atherosclerosis (10, 20). We know that in a human body leptin is able to induce the expression of cytokines – IL-6 and TNF-α by monocytes, enhance proliferation and activation of circulation T-lymphocytes, modulate monocytic-macrophage function and regulate the pro-inflammatory reaction (14). However, there is also evidence about leptin›s preventive role from the development of insulin-resistance and its anti-atherogenic effect (3).

The analysis of referred scientific works testifies, that inflammation is actively involved in the realization of immune response to atherosclerosis, whereas mediators of cellular connectivity such as cytokines TNF-α, and adipokine leptin play a significant role in it. Nevertheless, there remain some important problems to solve: which marker possesses the maximal prognostic ability in process destabilization? Is it reasonable to determine several markers or to do with only one, which best of all reflects the nature of the disease course? Up to now there is not a unilateral opinion about the nature and degree of inflammatory reaction, which would enable to stratify ore refer patients to the high risk group of possible CV complications.

The aim of the research – to study plasma concentration and correlation of inflammation biomarkers CRP, TNF-α and leptin level in IHD-patients with various disease course and to define their diagnostic validity as indicators of destabilizing the atherosclerotic process.

Patients and methods

Taking into account all possible gender variations of biochemical factors, only men with IHD (86 persons with average age of 56.24 ± 5.12 years) were in focus of the study, including 60 patients with stable ischemic heart disease (SIHD) and 26 patients with unstable ischemic heart disease (UIHD). 29 patients with SA showed functional class (FC) II, 31 patients showed FC III.

Thirty-eight patients with SIHD and 15 patients with UIHD had the old myocardial infarction (MI) in the

anamnesis (over 1 year before). The criterion for choosing patients for the research was the presence of confirmed IHD diagnosis. Prior to the research, screening thorough complaints and anamneses gathering, obtaining patient's informed agreement to participate in the research had been performed in conformity to the ethic norms of the Helsinki Declaration.

The diagnosis of stable IHD was set in accordance with the Guidelines of the European Society of Cardiology (2013) (16). All the patients underwent examinations for angina pectoris syndrome, electrocardiography (ECG) in 12 abductions in rest, Daily (Holter's) ECG monitoring, bicycle ergometry test (BET) at absent contraindications, echocardiography (EchoCG); coronary angiography was performed for 52 out of 60 patients (86.7%). Post-infarction cardiosclerosis was diagnosed from the anamnesis, confirmed by the medical documentation and typical changes in ECG and EchoCG.

The diagnosis of UA was based on the clinical findings with absence of steady changes of ST segment or deflection T in ECG, as well as with absence of slight increase of MB fractions of creatinephosphokinase (MB-CPK) and troponin T levels in blood. Coronary angiography was made to 21 (80.8%) patients with UIHD. The development of the subsequent UIHD attack of the patients under study was traced no later than on the 5^{th} day before hospitalization.

Patients with acute and chronic inflammation processes, liver or kidney dysfunctions, decompensated diabetes mellitus, thyroid gland diseases, obesity degree 3-4, chronic impaired cardiac function III-IV FC, infectious and oncological diseases were not included into the research. The basic therapy included antithrombotic agents, statins, beta-blockers, nitrates (when necessary), and inhibitors of angiotensin-converting enzyme (IACE); at UIHD the double antithrombotic and anticoagulation therapy was performed additionally.

The control group included 26 healthy male volunteers of the matching age (about 55.37±4.82 years old), who underwent BET and a number of other studies to exclude IHD. The standard examination of patients involved in an inquiry, physical examination, determining anthropometric values, body mass index (BMI), recorded ECG in 12 abductions, clinical blood, urine tests, biochemical blood tests for the levels of glycose, alanine aminotransferase (ALT), aspartate aminotransferase (ACT), bilirubin (fractionally), creatinine, urea, electrolytes (K^+, Na^+), determining blood lipid spectrum (overall cholesterol level, and low-density lipoproteins cholesterol and high-density lipoproteins cholesterol, triglycerides), enzymes – MB-CPK, troponins T and I.

Plasma levels of highly sensitive CRP, TNF-α (hs-CPP, hs-TNF-α) and leptin were determined by immune-enzyme methods (IEM) with the help of appropriate reagent kits: "hs-CRP ELISA" ("DRG", USA), "TNFα ELISA test kit" ("Diaclone", France) and "Leptin ELISA" ("DRG Diagnostics", Germany).

The statistical analysis of the obtained results was carried out with the kit of software Microsoft Excel, Statistica Windows 6.0. The methods of parametric and non-parametric statistics were used: the average values, their standard errors, median were computed, the correlation analysis according to Spearman, mono- and multifactor regression analysis were conducted (21).

Results

The determination of hs-TNF-α, hs-CRP and leptin levels in the control group enabled to identify referent and average values: for hs-CRP: 0.68 – 1.15 (0.78±0.04) mg/ml, for hsTNF-α: 1.04 – 1.35 (1.18±0.07) pg/ml for leptin: 8.11-12.56 (10.32±1.12) ng/ml (***table 1***), which corresponds with the majority of data obtained by other researches (1, 10, 11, 13, 20). Patients with IHD showed the increasing or increased levels of all studied values, the most significant changes were traced in patients with UIHD. The frequency analysis of valid increase of levels hs-CRP, hs-TNF-α and leptin showed that the group of UIHD-patients had a higher hs-CRP level in comparison with the referent values in 24 out of 26 examined persons (92.3%), the level of hs-TNF-α – in all persons (100%), leptin level in 22 persons (84.6%). The frequency of increase in plasma levels of inflammation and leptin indicators in patients with SIHD was slightly lower. Patients with severer course of the disease (FC III) showed a more frequent inflammation markers increase than those with FC II. Thus, the rise of hs-CRP level was traced in 26 of 31 (83.9%) patients with stable IHD FC III, the rise of hs-TNF-α level in 24 patients (77.4%), while patients with FC II showed the increase of hs-CRP in 22 of 29 (75.9%) and that of hs-TNF-α in 21 persons (72.4%). No significant differences in the frequency of leptin level increase in patients

Table 1. Plasma levels of hs-CRP, hs-TNF-α and leptin in patients with various clinical course of ischemic heart disease
Tabuľka 1. Plazmové koncentrácie hs-CRP, hs-TNF-α a leptínu u chorých s rôznym klinickým priebehom ischemickej choroby srdca

Values	Control group (n=26)	Stable ischemic heart disease				Unstable ischemic heart disease (n=26)	PP5-2	PP5-3	PP5-4
		The whole group (n= 60)	FC II (n=29)	FC III (n=31)	PP3-4				
	1	2	3	4		5			
hsSRP, mg/l	0.78±0.04	3.21±0.14*	2.60±0.21*	3.76±0.18*	<0.1	4.69±0.17*	<0.001	<0.001	<0.05
hsTNF-α, pg/ml	1.18±0.07	2.71±0.21*	2.37±0.18*	3.03±0.17*	<0.01	3.94±0.21*	<0.001	<0.001	<0.01
Leptin, ng/ml	10.32±1.12	18.28±0.92*	16.75±1.17*	19.73±1.24*	<0.05	21.42±1.02*	<0.05	<0.001	>0.05

Notes: 1 - * - credibility of value differences in comparison with the control group at p <0.05; 2 – P3-4, P5-2, P5-3, P5-4 – credibility of value differences between the patient groups under study.

with FC II and FC III angina pectoris were found: in 21 of 29 (72.4%) and in 23 of 31 (74.2%), correspondingly, p>0.05.

The data about the differences in the frequency of inflammation and leptin indicators rise at IHD of different nature and severity degree were confirmed at the analysis of average values of the studied indicators. Thus, average values of inflammation and leptin biomarkers of IHD-affected patients were reliably higher than those of the control group, increasing in progression alongside with the severity of the disease (***table 1***). The levels of hs-CRP and hsTNF-α in patients with FC III were significantly higher than those in patients with FC II angina pectoris, growing by 44.6% and 27.8% correspondingly. The differences of these indices in patients with SIHD FC III were also reliable (p<0.05), though the rise degree of hs-CRP appeared to be slightly lower 24.7%, the level of hs-TNF-α rose by 30.0%. Patients with SIHD FC III showed parallel significant increase of plasma leptin in comparison with FC II patients by 17.8% (p<0.05) (***table 1***). The greatest growth of all three indices was present in patients with UIHD, though the leptin level did not remarkably differ from the values in the group of FC III angina pectoris.

According to the studied scientific sources, the level of hs-CRP from 1.15 to 1.9 mg/l can be considered as a slight increase, from 2.0 to 3.0 mg/l - moderate increase, since it is associated with the average risk of cardiovascular failures; from 3.0 to 10.0 mg/l - significant increase, which enabled to refer these patients to a group of assigned risk (25). To evaluate the relevance of levels of hs-TNF-α and leptin as criteria of latent non-specific inflammation and heightened cardiovascular risk the changes in these indices in relation to the amount of hs-CRP were analyzed (***table 2***)

The obtained data testify to the fact, that as the content of hs-CRP increased, so did the levels of hs-TNF-α and leptin progressively reaching the highest value at hs-CRP ≥3.0 mg/l (***table 2***). Suffice it to mention the valid difference (<0.01) between the rates of the studied values (hsTNF-α and leptin) in various sub-groups singled out according to gradation degree of level hs-CRP: slight, moderate and significant.

The comparisons based on regression analysis enabled to determine the boundary criteria and to suggest with great probability about the activation of latent inflammation irrespective of presence or absence of clinical symptoms of process destabilization. To them refer the level of plasma hsCRP 2.57 mg/ml, the level of plasma hs-TNF-α 2.44 pg/ml, the amount of leptin in plasma 18.44 ng/ml.

We have also found quite a remarkable correlation between the leptin level, on the one hand, and the amount of hs-TNF-α and hs-CRP – on the other (r=0.59 and r=0.57, correspondingly, p <0.01) in patients with UA and r=0.50 and r=0.53, correspondingly, p <0.01 – in patients with stable IHD).

The comparative assessment of critical values of inflammation biomarkers in patients with stable and unstable course of IHD showed, that the probability of process destabilization grows when biomarkers level exceeds the stated values. Independent factors of destabilization of IHD were the levels hs-CRP >2.57 mg/l and hs-TNF-α >2.44 pg/ml.

The validity of the IHD-destabilization model increased remarkably at simultaneous use of these two markers: hs-CRP >2.57 mg/l and hs-TNF-α >2.44 pg/ml. Leptin level added to the mathematic model of IHD destabilization was less specific and did not influence its informative value.

We failed to find a valid correlation of overall cholesterol level (OCL) and LDL cholesterol to the levels of inflammation indicators both at stable and unstable process course. Patients with UIHD of correlation rate for hs-TNF-α made up r=0.19 and r=0.23, correspondingly, p >0.05 and for hs-CRP r=0.21 and r=0.20, p >0.05, correspondingly. The correlation between pro-atherogenic indices of lipid blood count and leptin level (r=0.17 and r=0.20, p >0.05, correspondingly) turned out to be invalid as well. At the same time we traced a valid inverse correlation between the level of HDL cholesterol and the amount of hs-TNF-α and hs-CRP (r= -0.39 and r= -0.35, correspondingly, p <0.05).

Discussion

The data obtained during the research can testify to the moderate, clinically not manifested activation of both systemic and local latent inflammation process and to the risk of destabilization of the atherosclerotic plaque with subsequent atherotrombosis.

The traced increase of inflammation indicators in patients with stable IHD probably manifests about moderate activation of inflammatory process in the vascular wall, the degree of which is insufficient for the clini-

Table 2. Plasma levels of hsTNF-α and leptin in relation depending on the level of hs-CRP
Tabuľka 1. Plazmové koncentrácie hs-TNF-α v závislosti od koncentrácie hs-CRP

Values	hs-CRP <1.15 mg/L	hs-CRP 1.15-1.9 mg/L	P1-2	hs-CRP 2.0-2.9 mg/L	P3-1	P3-2	hs-CRP ≥3.0 mg/L	P4-1	P4-2	PP4-3
	1	2		3			4			
hsTNF-α, pg/ml	1.37±0.11	2.03±0.16*	<0.01	2.73±0.13*	<0.001	<0.05	3.75±0.18*	<0.001	<0.01	<0.01
leptin, ng/ml	11.74±1.15	15.68±1.11*	<0.01	19.18±1.08*	<0.001	<0.01	22.75±1.14*	<0.001	<0.001	<0.01

Notes: 1 - * - the validity of value differences in comparison with the control group at p <0.05; 2 – P1-2, P3-1, P3-2, P4-1, P4-2, P4-3 - the validity of value differences between the patient populations.

cal manifestation of exacerbation. We can suggest that the increase of inflammation biomarkers level at patients with stable IHD characterizes individual immune inflammatory reaction of the organism, which being the basis, preconditions the destabilization of the IHD course (13).

The destabilization of the process is followed by the activation of the inflammatory reaction which is manifested in significant increase of levels of hs-TNF-α and hs-CRP by 24.7% and 30.0%, correspondingly ($p<0.05$). The leptin level grew at least by 8.6% ($p>0.05$).

The obtained correlations between the levels of inflammation indicators and the amount of leptin enable to suggest, that leptin is a biologically active combination, produced by the fatty tissue which does not only contribute to the regulation of lipid and carbohydrates metabolism, but also influences the processes of inflammation and thrombosis, participating in pathogenesis of atherosclerosis and its complications, according to findings of numerous researchers (10, 14, 20).

CRP's direct contribution in plaque destabilization can be preconditioned by its ability to stimulate metalloproteinases production by inflammatory cells (24). We can suggest that the prognostic significance of CRP level in plasma of IHD-patients is determined by the presence of its direct relation to the state of atherosclerotic plaque. Thus, autopsy of 302 sudden mortality cases showed the average CRP level of 3.2 mg/l at acute plaque rupture, 2.9 mg/l – at plaque erosion, 2.5 mg/l - at stable plaque and 1.4 μg/ml - in the references values (5).

TNF-α stimulates the synthesis of proteins of acute inflammation phase and is a binding factor of inflammation and pro-atherogenic disorders of lipid metabolism, leading to the onset of hypertriglyceridemia. The increasing systemic production of TNF-α can be regarded as one of the important determinants of IHD destabilization.

The absence of valid correlations between the levels of pro-atherogenic fractions of lipoproteins and biomarkers supports the current view about the absence of direct dependence of destabilization of atherosclerotic process on the blood lipid levels. The obtained negative associative correlations between the level HDL cholesterol and inflammatory markers somehow prove the decrease of anti-inflammatory activity of HDL in IHD-patients, which corresponds with the views of other authors (4).

Changes of the blood cytokines profile at the development of acute coronary syndrome (ACS) can be explained by the fact, that a high intensity of inflammatory process in the vulnerable to disintegration plaque is determined by the presence of activated macrophages in it, which release pro-inflammatory cytokines TNF-α, IL-6, and the low number of P-cells as the main producer of anti-inflammatory cytokine IL-10 (9, 19). Thus, the changes in markers typical for inflammation in IHD-patients are associated with the phase course of atherosclerosis, exacerbation and remission periods, and the extent of vascular involvement into the inflammatory process.

Conclusions

The variation of biochemical indicators of nonspecific inflammation intensity is associated with the peculiarities of the disease course and its severity. Nonspecific systemic inflammatory reaction is present not only at ACS, but also at stable ischemic heart disease.

The levels hs-CRP >2.57 mg/l and hs-TNF-α >2.44 pg/ml are independent prognostic factors of IHD destabilization and the risk of adverse events at clinically stable disease course. The plasmatic leptin level is of minor importance in detecting process destabilization.

The combination of levels hs-CRP >2.97 mg/l and hs-TNF-α >2.44 pg/ml possesses the most capable of predicting atherosclerosis destabilization and development of cardiovascular complications in patients with stable ischemic heart disease.

The determining plasma markers of chronic latent vascular wall inflammation - hs-CRP, hs-TNF-α and hormone of fatty tissue leptin acting like cytokine irrespective of the presence or absence of atherogenic dyslipidemia, enables to detect persons at high risk of onset and development of atherosclerosis, IHD and atherothrombotic complications and determines the need to optimize prevention and treatment.

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