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ABSTRACTS

Results of the Russian research program on the diagnosis and treatment of patients with familial hypercholesterolemia. High prevalence, low awareness, poor adherence

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Resume

Goal. The true prevalence of familial hypercholesterolemia (FH) in the Russian Federation is unknown. The purpose of this study was to assess the possibility of timely detection of this disease and the effectiveness of therapeutic and diagnostic measures in persons with severe hypercholesterolemia.

Materials and methods. Between December 2013 and December 2016, 1027 patients with a total cholesterol level (OC) ≥ 7.5 mmol/l and/or a low-density lipoprotein cholesterol (LDL) cholesterol ≥ 4.9 mmol/l were included in the leading and regional medical centers, which formed the basis for the organization of the work of the national multicenter register on the FH (Register of FH). Information on patients was recorded in the electronic medical system and contained

data on the evaluation of the clinical status and risk factors of atherosclerosis, blood lipid parameters, echocardiography and duplex scanning of brachiocephalic arteries, and data on treatment conducted for the control of blood lipids.

Results. Mean blood lipid levels were: OC 9.2 ± 2.0 mmol/l, LDL cholesterol 6.3 ± 1.7 mmol/l, lipoprotein (a) Lp (a) 37 ± 44 mg/dl. Elevated levels of Lp (a) (more than 30 mg/dl) were detected in 38% of individuals. In the presence of a pronounced primary hypercholesterolemia, the probability of detection of the FH reaches 20%. For an accurate diagnosis it is sufficient to apply a simple examination complex based on the modified criteria of the Dutch lipid clinics. The frequency of prescribing lipid-lowering therapy does not exceed 25%, reaching the target level of LDL cholesterol is extremely low. The true prevalence within the project is impossible to assess, because many centers included patients with a known or probable diagnosis of the FH. With a view to timely diagnosis and treatment, increasing the doctors' awareness of the FH, the National Society for the Study of Atherosclerosis has developed short recommendations on the diagnosis and treatment of FH and methodological recommendations on the organization of medical care for patients with hereditary atherogenic impairments of lipid metabolism.

Conclusion. Family hypercholesterolemia in Russia is distinguished by untimely diagnosis at high prevalence, low awareness of doctors and patients about the disease, poor adherence to lipid-lowering therapy with an extremely rare achievement of the target level of LDL cholesterol.

Keywords: familial hypercholesterolemia, registry, atherosclerosis, prevention.

Obesity and resistant hypertension

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Abstract

Obesity is the strongest risk factor for resistance to drug therapy in hypertensive patients, which is caused by a substantial number of pathophysiological mechanisms. One of them is dysregulation of adipokines – peptides produced by a fat tissue; adiponectin is one of them, today it attracts the most attention. Another pathological pathway of development of refractoriness to hypotensive drugs is impairment in regulation between renin-angiotensin-aldosterone (RAAS) and natriuretic peptide (NP) systems, especially in patients with visceral obesity. Pharmacological enhancement NP actions may cause an additive benefit to effects of the RAAS inhibition. Currently ARNI, a novel drug combination of valsartan (angiotensin II receptor inhibitor) and sacubitril (inhibitor of neutral endopeptidase neprilysin, that catalysis the intracellular degradation of NP) is widely discussed in scientific society. Another component of RAAS – aldosterone also plays an important role in development of resistant hypertension in obese people: it has been shown that hyperaldosteronism is a strong risk factor of metabolic syndrome and refractoriness to hypotensive drugs. Further, it is well known, that chronic hyperactivation of sympathetic nervous system often occurs in obese patients with resistant hypertension. The novel non-pharmacological method of renal denervation and a bunch of SYMPLISITY HTN trials will be briefly reviewed. In conclusion specific features of pharmacological treatment of hypertension in obese people, possible side effects of antihypertensive drugs that may affect overweighted patients will be discussed, as well as an impact of weight-reducing drugs in people with hypertension.

Keywords: resistant hypertension, obesity, adipokines, natriuretic peptide, hyperaldosteronism, renal denervation, weight-reducing drugs.

Role of combined determination of troponin and copeptin in diagnosis and prognosis in acute coronary syndrome with non

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Summary: This literary review are the modern data on the clinical, laboratory and instrumental diagnostics in patients with acute coronary syndrome. Presented in detail and the role of the new target biochemical marker copeptin (C-end part of the Pro-vasopressin), in the diagnosis and prognosis in patients with acute coronary syndrome (ACS) with Non-ST-Elevation. According to the literature data for acute myocardial infarction (AMI) copeptin level rises immediately after the onset of symptoms, reaching peak values during 3-4 hours and it is expected that together with copeptin measurement troponin T and I may constitute a valuable prognostic information for risk stratification and outcome in patients with Non-ST-Elevation ACS.

st segment elevation

Keywords: acute coronary syndrome, myocardial infarction, troponin T and I, copeptin, cardiovascular risk, diagnosis, prognosis.

Left ventricular myocardial perfusion in patients with hypercholesterolemia during statin therapy

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Abstract

Aim: To evaluate the effect of statin therapy on myocardial perfusion assessed with single-photon emission computed tomography (SPECT) with ^{99m}Tc -MIBI in asymptomatic patients with severe hypercholesterolemia (HCh).

Materials and Methods: The study included 60 patients with total cholesterol levels >7.5 mmol/L and/or LDL cholesterol >4.9 mmol/L, without clinical signs of ischemic heart disease. All patients, as well as 20 healthy volunteers, underwent myocardial ^{99m}Tc -MIBI rest/stress SPECT with CT-attenuation correction. Standard quantitative perfusion parameters (rest/stress/reversibility extents, SRS, SSS, SDS) were evaluated, as well as two new parameters of perfusion defects severity (σ_{sev}) or heterogeneity (σ_{het}). The dynamics of initial perfusion impairments and inhomogeneity in patients, receiving statin for 1 year, was compared with noncompliant patients.

Results: Quantitative assessment of initial impairments and inhomogeneity of left ventricular myocardial perfusion with SPECT using proposed σ_{sev} and σ_{het} parameters reflects expert visual interpretation better than standard parameters. Patients with HCh demonstrate more severe inhomogeneity of MIBI uptake in the LV myocardium, compared with the control group, Rest $\sigma_{\text{het}} = 6.5 \pm 1.2$ and 5.9 ± 0.9 , respectively, $p < 0.01$). Positive correlation between Rest $\sigma_{\text{sev}}/\sigma_{\text{het}}$ was observed with TCh/LDL-C levels ($r = 0.33$, $p < 0.01$; $r = 0.37$; $p < 0.01$; $r = 0.29$; $p = 0.02$; $r = 0.32$; $p = 0.01$). Connections of perfusion quantitative parameters with HDL-C/TG were not revealed. In compliant group of patients, visual deterioration of LV myocardial perfusion was noted in 18% of cases, in noncompliant group - in 35%, delta of stress σ_{het} parameter was -0.2 ± 1.6 and 0.7 ± 1.6 , respectively ($p = 0.05$).

Conclusion: In patients with severe hypercholesterolemia initial myocardial perfusion impairments or inhomogeneous perfusion is visually observed, which can be quantified using σ_{sev} and σ_{het} parameters. Statin therapy provides less pronounced worsening of initial perfusion impairments than in noncompliant patients.

Keywords: SPECT, myocardial perfusion, hypercholesterolemia, statins, quantitative methods.

Analysis of the long-term results of surgical treatment of patients with multifocal atherosclerosis in different age groups

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Summary

Purpose. The study of long-term results staged reconstructive operations on coronary and non-coronary arterial basins in patients with multifocal atherosclerosis (MFA) in different age groups.

Material and methods. It was included 764 consecutive patients (655 men and 109 women) aged 39 to 84 years with MFA, who underwent isolated coronary artery bypass grafting (CABG) or CABG in combination with simultaneous or staged surgical interventions in the non-coronary vascular beds. The treatment procedure was defined by the heart team with the inclusion of cardiovascular surgeons, cardiologists and anesthesiologists. Depending on the age of patients formed 4 groups: Group 1 - patients up to 60 years (n=338), 2 group - 60-64 years (n=185), 3 group - 65-69 years (n=137) and group 4 - patients 70 years and older (n=104).

Results. Long-term results after reconstructive operations on various vascular regions analyzed in 85.3% of patients, and the median follow-up was 47.8 ± 21.7 months. Total mortality, mortality from cardiovascular disease and other causes increased with age, but not observed statistical significance between the groups. The groups also did not differ between themselves and the number of recurrent angina (p=0.217), myocardial infarction (p=0.311) and stroke \ TIA (p=0.161).

Conclusion. The use of differentiated surgical approach proved safe and effective in patients with MFA regardless of age, which is confirmed by long-term results obtained are comparable with findings in younger patients.

Keywords: advanced age, coronary artery bypass surgery, multifocal atherosclerosis, long-term results.

Adherence to lipid lowering therapy in post-ACS patients during 3 years follow up

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Abstract

Objective: to evaluate long-term efficacy and adherence to therapy with statins in patients with acute coronary syndrome (ACS).

Material and methods: In a register-based retrospective study included 458 patients with ACS. During hospitalization 257 (56.1%) patients underwent successful percutaneous coronary intervention (PCI). At 148 (32.3%) patients at admission to the hospital revealed renal dysfunction (RD) – glomerular filtration rate (GFR <60 ml/min/1.73 m², 75 (16.4%) – diabetes mellitus (DM). Statin for the first year of observation took 63.3% (n=290) from all included patients. After determination of compliance a year after the ACS assessed the incidence of "endpoints" within the next two years of observation. Revealed that the frequency of two-year cardiovascular mortality was 8.1% (n=37), and the total mortality 9.6% (n=44).

Results: the 4 comparison groups based on treatment strategies and the presence or absence of RD. In the I group included 184 patients without RD and with successful PCI; in II – 73 patients with RD and PCI; III – 126 of patients without RD and with a conservative treatment strategy; IV – 75 patients with RD and initial conservative treatment strategy, which survived to the 12th month of observation. The acceptance of statins in group IV reduced the relative risk (RRR) of cardiovascular death within two years of follow-up to 88.3% (p=0.01). In the I group therapy significantly (p=0.01) was associated with a decrease in General (RRR=71.5%), but not cardiovascular, mortality. In groups II and III revealed only a tendency to decrease the frequency of "end points" for 24 months in patients receiving statins. In patients with diabetes receiving statins were less effective than in patients without diabetes. Thus, the RRR for total and cardiovascular death in patients without DM was, respectively, at 62.8% (p=0.003) and 66.0% (p=0.003).

Conclusion. We identified groups of patients with different efficacy of statin therapy. Only 2/3 of patients during the year after ACS took statins and a reduction in the frequency of their admission was associated not only with aging but also with failure as coronary angiography during hospitalization, and surgical myocardial revascularization in the three years of observation. All of the above facts dictate the need to study such patients additional opportunities to improve prognosis and adherence to therapy (e.g., added to statin therapy, PCSK9 inhibitors).

Keywords: acute coronary syndrome, statins, prognosis.

New pleiotropic effects of statins: implications for telomerase activity and telomere length

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Abstraction.

The results of clinical studies conducted in recent times, suggest that statins have a number pleiotropic effects, among which a special attention deserves the ability to slow the rate of telomere erosion and increase telomerase activity. It is known that telomeres are the biological marker of aging. Thus, it can be assumed that statins are potential geroprotectors, because this group of drugs is one side influencing the overall mortality by decreasing the risk of developing cardiovascular diseases, but on the other hand, slows down the aging process, influencing his cause.

The following review analyzes studies indicating that associative links between taking statins, the rate of telomere shortening and telomerase activity.

Keywords: statins, aging, telomeres, telomerase, cardiovascular diseases.

Comparative evaluation of symmetric and asymmetric ischemic mitral regurgitation according to the three-dimensional transesophageal and two-dimensional transthoracic echocardiography

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Abstract

The development and progression of chronic ischemic mitral regurgitation (IMR) is associated with mitral tethering phenotype determined by localization of myocardial infarction (MI).

Purpose. To evaluate three-dimensional (3D) mitral valve (MV) parameters in symmetric and asymmetric mitral regurgitation (MR) and analyze correlations with MR severity, left ventricle (LV) global and local remodeling.

Methods. 43 patients with chronic IMR underwent 3D transesophageal and two-dimensional (2D) transthoracic echocardiography. Occlusion of one or more coronary arteries was diagnosed in 100% (n=43) of patients.

Results. In asymmetric IMR, caused by inferoposterior MI tenting area significantly increases, tenting volume is also enlarged, but less in size than in symmetric type. In asymmetric MR 3D MV geometry changes are affected by local LV remodeling (i.e. apical displacement of posteromedial papillary muscles [ADPM PM]) that causes restriction of MV posterior leaflet. Posterolateral angle in asymmetric pattern is explicitly associated with ADPM PM and IMR severity. This fact reflects predominantly systolic restriction of posterior leaflet on one hand and on the other indicates involvement of MV dysfunction mechanism in MR progression. In symmetric IMR MV geometry changes in greater degree than in asymmetric one depend on LV dilatation and ejection fraction reduction.

Comparative analysis shows significant differences of 3D MV parameters in two MR phenotypes.

Conclusions. 3D MV geometric and functional alterations, global/local LV remodeling and regurgitation severity significantly differ in symmetric and asymmetric MR. 3D MV geometry and function changes are associated with MR phenotype determined by MI localisation.

Keywords: ischemic mitral regurgitation, three-dimensional mitral valve parameters, symmetric and asymmetric.

A rare genetic mutation in patients with heterozygous familial hypercholesterolemia.

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Abstract

Familial hypercholesterolemia (FH) is a rare disease, although its occurrence according to the Russian by FH register higher than previously thought. Often this pathology is not revealed during the examination of patients, due to poor awareness of physicians. Diagnosis is based on a certain phenotype and genetic studies. This article describes a clinical case of heterozygous FH patient without clinical manifestations, diagnosed on the basis of screening. This patient was found a rare mutation in the APOB gene.

Keywords: heterozygous familial hypercholesterolemia, APOB mutation, screening for familial hypercholesterolemia.

Relative abundance of animal protein in diet: the initiator of the atherosclerotic process

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Abstract

In the presented atherosclerosis genesis and development hypothesis relative abundance of animal protein in diet is assumed as the initiator of the process.

Relative abundance of dietary protein causes exhaustion of ornithine cycle resources in hepatocytes. Unreacted ammonia (NH₃) inhibits ferments of the respiratory chain; electrons transmit directly to oxygen, and reactive oxygen species (ROS) develop in hepatocytes. It results in lipid peroxygenation in cells of endothelial reticulum and in apolipoproteins conformational changes. From hepatocytes oxidized VLDL and oxidized HDL containing active malondialdehyde (MDA) release into blood. Apo-B100, apo-C-II, and apo-A-I conformational changes cause development of dyslipidemias.

MDA of oxidized lipoproteins damages membranes of endotheliocytes with endothelial dysfunction genesis. Oxidized apolipoprotein apo-B100 provokes the immune-inflammatory response in the vessel wall. During a longtime receiving of oxidized lipoprotein apo-B100, foam cells develop as well as atherosclerotic changes with their progression leading to angina pectoris and myocardial infarction. MDA of oxidized lipoproteins also damages membranes of erythrocytes and those of thrombocytes causing microcirculation disorder in tissues and enhanced adhesion respectively.

The presented hypothesis covers all the main stages of atherogenesis.

Keywords: relative abundance of animal protein, ammonia (NH₃), respiratory chain, reactive oxygen species, lipid peroxygenation, apolipoproteins, MDA, ox-VLDL, ox-HDL, intima endothelium, immune inflammation, endothelial dysfunction, dyslipidemias, atherosclerosis, myocardial infarction.

Pitavastatin is a modern statin for the correction of dyslipidemia and the risk of cardiovascular complications. Resolution of the expert council

Expert council: A. Catapano¹, V.V. Kukharchuk², I.V. Sergienko², M.V. Ezhov², A.V. Susekov², S.R. Gilyarevsky³, S.Yu. Martsevich⁴, I.I. Chukaeva⁵

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