

**Atherosclerosis and Dyslipidaemias**  
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**ABSTRACTS**

**Excessive formation of advanced glycation end-products as a possible cause of increased risk of restenosis after coronary stenting in patients with diabetes mellitus**

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**Abstract**

Patients with diabetes mellitus are at increased risk of restenosis after coronary artery stenting. Chronic hyperglycemia is associated with advanced glycation end products excessive production. There are data that in-stent restenosis in patients with diabetes mellitus may be related to plasma level of advanced glycation end products. One of the reasons for this is that protein glycation by alteration of protein structure adversely affects their function. Another cause may be due to the interaction between advanced glycation end products and membrane-bound receptor for advanced glycation end-products. Experimental data indicate that blockade of receptor for advanced glycation end-products with soluble receptor for advanced glycation end-products resulted in significantly decreased of neointimal expansion after arterial injury.

**Keywords:** restenosis, diabetes mellitus, advanced glycation end products, receptor for advanced glycation end products.

**Atherosclerosis. Understanding and Solutions Finding**

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**Abstract**

One of the major human diseases is atherosclerosis with a lot of very aggressive clinical masks. Modern science has been able to create a large number of distinct theories to explain the origin and development of this disease, but the practical success has not yet been achieved. The author believes that it is impossible to find out the true nature of atherosclerosis relying on the modern method of research – clinical and anatomic mapping (CAM) method. It is necessary to make a major revision of the scientific approach to the study of any pathology. It is suggested to pay attention and assess the possibilities of systemic analysis, in particular the academician P. K. Anokhin's functional system (FS) theory.

**Keywords:** atherosclerosis, clinical and anatomic mapping method, academician Anokhin's functional system theory, basic concept change.

**Review on the article «Atherosclerosis. Understanding and Solutions Finding» by V. S. Hazov**

V. V. Kukharchuk, Editor-in-Chief of the Journal of Atherosclerosis and Dyslipidaemias

**Replacing one lipid-lowering drug by the other: the pros and cons with prolonged ambulatory monitoring**

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**Abstract**

**Aim.** Long term administration of lipid-lowering drugs is one of the important and key moments in the outpatient management. This paper analyzes the results of lipid-lowering therapy and replacement of lipid-lowering drugs by another in an outpatient practice, as well as the effectiveness of this replacement in patients with cardiovascular disease. The aim was to analyze the dynamics of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), highdensity lipoprotein cholesterol (HDL-C), triglycerides (TG), when changing lipid-lowering therapy in a real outpatient practice.

**Materials and methods.** The study included 163 patients with high/very high risk of cardiovascular events (on a scale SCORE) (HRCVE group) and 173 patients with coronary artery disease (CAD group). The study was open. All patients were taking rosuvastatin as a lipid-lowering drug during the first year of observation, which was issued free of charge. After 1 year of treatment rosuvastatin was replaced by atorvastatin, which was given for free by local doctors. Some of the patients did not want to change drug and remained on rosuvastatin therapy at their own expense. The patients also received other medical treatment according to indications (beta-blockers, angiotensin-converting-enzyme inhibitors, calcium channel blockers, diuretics and nitrates). Instrumental and laboratory tests (clinical examination, electrocardiography, blood chemistry) were performed at baseline, after 12 and 24 months of statin therapy.

**Results.** Lipid-lowering therapy for 24 months was well tolerated by patients. A significant reduction in TC, TG, LDL-C and an increase in HDL-C were observed in two groups of patients in a year. A statistically significant adherence increase to the therapy in both groups and improve of patients' life quality were also found. One year after rosuvastatin was changed for atorvastatin there was a statistically significant increase in the level of TC ( $p = 0.004$ ) and LDL-C ( $p = 0.002$ ) in CAD group of patients. In the group with high/very high risk of the same pattern an increase of TC and LDL-C ( $p = 0.0007$  and  $p = 0.00008$ , respectively) was observed. TG and HDL-C were not significantly changed. In the rosuvastatin group the levels of TC, TG, HDL-C did not change, however, a slight, but statistically significant increase in LDL-C levels in both groups ( $p = 0.0009$  and  $p = 0.04$  respectively, in the group of HRCVE and the group of CAD) was found. No statistically significant changes in terms of aspartate aminotransferase, alanine aminotransferase, creatine kinase in both groups were observed.

**Conclusion.** The results showed high efficacy and good tolerability of long-term lipid-lowering therapy in both patients with CAD and with high/very high risk of CAD in the outpatient setting. When a high efficacy of one lipidlowering drug is achieved the change for other drug in an outpatient setting may lead to a decrease of treatment efficacy.

**Keywords:** lipid-lowering therapy, adherence to therapy, cardiovascular disease, hypertension, long-term therapy, outpatients.

## **Pluronic F-127-induced experimental dyslipidemia as a model for the revealing of a connecting link between immune response regulation and cholesterol metabolism**

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### **Abstract**

**Aim.** Abundant clinical and experimental evidences show that varied immunopathological processes are associated with disturbed cholesterol metabolism. The mechanism of this link is still understood incompletely and invites further investigation.

**Results.** It was demonstrated that pluronic F-127 (poloxamer 407)-induced dyslipidemia in mice is accompanied by the shift of Th1/Th2-balance which affects the intensity of immune reactions.

**Conclusion.** It was concluded that the administration of pluronic F-127 to animals is usable as an adequate laboratory model for the revealing of a connecting link between immune response regulation and cholesterol metabolism. The hypothetical mechanism of this connection involving the modulation of liver X receptors activity is discussed.

**Keywords:** cholesterol, immune reactions, pluronic F127, poloxamer 407, graft versus host reaction, GvHR, Th1/Th2-balance, nuclear receptors LXR.

## **The polymorphisms of apolipoprotein E and lipoprotein lipase genes in evaluating the effectiveness of the hypocaloric standard diet in obese patients**

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### **Abstract**

**Aim.** Aim of the study is to evaluate the effectiveness of the hypocaloric standard diet therapy for various polymorphic variations of lipoprotein lipase (LPL) and apolipoprotein E (ApoE) genes in obese patients.

**Materials and methods.** The study involved 110 obese patients with different allelic variants of ApoE and LPL genes. Lipid metabolism evaluation and analysis of  $\epsilon 2$ ,  $\epsilon 3$ ,  $\epsilon 4$  polymorphic alleles of ApoE gene and Ser447Ter of LPL gene using polymerase chain reaction are performed. The concentrations of total cholesterol (TC), triglycerides (TG), low density lipoproteins (LDL), high density lipoproteins (HDL) are measured by turbidimetry and spectrophotometry by using an automatic analyzer ConeLab60i (Finland).

**Results.** We concluded that the effectiveness of dietary intervention in lipid and carbohydrate metabolism disturbances in obese patients significantly higher in  $\epsilon 3/\epsilon 3$  genotype of ApoE gene (19 % reduced TC, 18 % – TG, 17 % – LDL, 20 % – HDL, 7 % – glucose),  $\epsilon 2/\epsilon 3$  genotype of ApoE gene (20 % reduced TC, 23 % – TG, 15 % – HDL) and in Ser447Ser genotype of LPL gene (17 % reduced TC, 21 % – TG, 14 % – HDL, 16 % – of LDL, 8 % – glucose).

**Conclusion.** Thus, the definition of ApoE and LPL gene polymorphisms can be used as a prognostic test in patients with an overweight and for developing of a personalized diet therapy in obese patients.

**Keywords:** obesity, diet, lipids, polymorphism.

## Coronary bypass grafts patency assessment using multislice computed tomography in the early and late periods after bypass surgery

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### Abstract

**Aim.** To evaluate the possibilities of multislice computed tomography (MSCT) in coronary bypass grafts patency assessment in patients with high surgical risk in early and late postoperative period. To determine the high risk time period for coronary bypass grafts occlusion.

**Materials and methods.** 185 patients with multivessel coronary artery disease and high surgical risk were included in the study. All patients underwent MSCT-angiography in 1.5–3 months and 9–12 months after coronary bypass grafting.

**Results.** 327 coronary bypass grafts (244 venous and 83 mammary) were analyzed. 1 mammary graft occlusion and 53 venous grafts occlusion, 16 significant stenoses and 5 nonsignificant stenoses were detected in 1.5–3 months after surgery. In 9–12 months after coronary bypass grafting 23 venous grafts occlusion and 1 significant stenosis were detected in addition to first computed tomography study. No new occlusion and significant stenosis were found in the second study.

**Conclusions.** Most of coronary bypass graft occlusions and stenoses were found in 1.5–3 months after surgery comparing with 9–12 months time period. The study showed high frequency of venous grafts stenoses and occlusions comparing to mammary grafts.

**Keywords:** multislice computed tomography, MSCT, CT-angiography, coronary angiography, coronary bypass surgery, coronary heart disease.

## Oxidized low-density lipoproteins and antibodies against oxidized low-density lipoproteins in patients with coronary atherosclerosis and healthy individuals

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### Abstract

**Purpose.** To determine the role of oxidized low-density lipoproteins (OxLDL) and antibodies against oxidized lowdensity lipoproteins (anti-OxLDL) in immuno-inflammatory process in patients (pts) with coronary atherosclerosis.

**Methods.** Three groups of male pts aged from 28 to 68 years were included in the study: healthy pts group without coronary heart disease (n = 10); a group with initial coronary arteries' atherosclerotic lesions (<50 %, n = 20) and group with angiographically documented severe coronary stenosis (>50 %, n = 50). Serum OxLDL and anti-OxLDL were identified by immune-enzyme analysis using MDA-oxLDL and OLAB IgG Biomedica commercial kits.

**Results.** There were not significant differences in OxLDL levels between these groups of pts (p > 0.3), but anti-OxLDL titers in healthy pts group were significantly higher compared to the pts with severe coronary stenosis (p = 0.03). SYNTAX Score was used to assess the severity of

coronary lesions in group of pts with severe coronary atherosclerosis. The anti-OxLDL titers was significantly higher in pts with SYNTAX index below the average median ( $p = 0.03$ ).

**Conclusion.** We didn't found significant evidence of association between OxLDL levels and coronary atherosclerosis in our clinical study. However, anti-OxLDL titers in healthy pts group were higher than in pts with severe coronary atherosclerosis. Among the pts with severe coronary atherosclerosis, a higher level of anti-OxLDL was observed in patients with a lower coronary lesions severity.

**Keywords:** atherosclerosis, oxidized low-density lipoproteins, antibodies against oxidized low-density lipoproteins, inflammation.

## Features of left ventricular myocardial perfusion in patients with hypercholesterolemia

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### Abstract

**Aim.** To evaluate left ventricular myocardial perfusion patterns, assessed with single-photon emission computed tomography (SPECT), in asymptomatic patients with severe hypercholesterolemia (HCh).

**Materials and Methods.** The main group included 26 patients with total cholesterol level  $>7.5$  mmol/l and/or high density lipoprotein cholesterol (LDL-cholesterol)  $>4.9$  mmol/l, with no clinical signs of coronary artery disease. All patients, as well as 10 healthy volunteers, underwent myocardial  $^{99m}\text{Tc}$ -MIBI (4.2-methoxy-isobutyl-isonitrile) rest/stress SPECT with CT (computer tomography) – attenuation correction. Standard quantitative perfusion parameters (rest/stress/reversibility extents, SRS, SSS, SDS) were evaluated. In addition, two new parameters for perfusion defects severity ( $\sigma_{\text{sev}}$ ) or perfusion heterogeneity ( $\sigma_{\text{het}}$ ) assessment were calculated.

**Results.** Stress test results were negative in 73 % of HCh patients. SPECT revealed no reliable reversible/irreversible perfusion defects, though inhomogeneous MIBI distribution was visually detected in 23 HCh patients (88 %). Standard perfusion parameters showed no reliable difference between two groups: rest extent was 8.3 (5.0–11.0) and 7.3 (4.5–9.1),  $p > 0.05$ ; stress extent – 11.3 (6.5–14.0) and 6.3 (4.2–9.7),  $p > 0.05$ ; reversibility extent – 5.0 (2.5–8.0) and 5.5 (3.1–8.4),  $p > 0.05$ ; Summed Rest Score (SRS) – 3.5 (2.0–5.5) and 0.5 (0.0–1.5),  $p > 0.05$ ; Summed Stress Score (SSS) – 7.3 (4.5–9.5) and 4.8 (2.4–6.7),  $p > 0.05$ ; Summed Difference Score (SDS) – 2.5 (2.0–6.0) and 4.3 (0.5–6.5),  $p > 0.05$ ; while some  $\sigma_{\text{sev}}/\sigma_{\text{het}}$  parameters were reliably higher in HCh patients: rest  $\sigma_{\text{sev}}$  – 25.4 (22.0–28.3) vs. 21.1 (18.2–23.2),  $p = 0.06$ ; rest  $\sigma_{\text{het}}$  – 7.8 (6.9–8.7) vs. 4.7 (4.0–5.8),  $p = 0.03$ ; stress  $\sigma_{\text{het}}$  – 8.2 (7.2–8.9) vs. 5.3 (3.4–6.7),  $p = 0.03$ , respectively.

**Conclusion.** In patients with severe hypercholesterolemia initial myocardial perfusion impairments or inhomogeneous perfusion is often observed. However, standard perfusion parameters values show no reliable difference in those patients when compared to healthy volunteers. New  $\sigma_{\text{sev}}/\sigma_{\text{het}}$  parameters are more suitable for assessment of initial myocardial perfusion impairments that are visually observed in HCh patients.

**Keywords:** single-photon emission computed tomography, SPECT, myocardial perfusion, hypercholesterolemia, quantitative methods.

# **Clinical case of skin lesions in the form of eruptive xanthomas in a patient with mixed hyperlipidemia**

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## **Abstract**

Patients with eruptive xanthomatosis on the skin usually go to physicians, dermatologists, or maybe to cardiologists, endocrinologists. The presence of xanthomas on patient's skin is an indication to determine the levels of total cholesterol and triglyceride. The article presents a clinical example of diagnostics and treatment of a patient with eruptive and tuber-eruptive xanthomatosis with high hyperlipidemia.

**Keywords:** eruptive xanthomatosis, tubero-eruptive xanthomatosis, mixed hyperlipidemia, hypertriglyceridemia.