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PECULIARITIES OF COMPLIANCE IN THE CORRECTION OF THE COMPONENTS OF METABOLIC SYNDROME IN RECURRENT MYOCARDIAL INFARCTION

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Metabolic syndrome (MS) and such its components as type 2 diabetes mellitus (T2DM), obesity, dyslipidemia, arterial hypertension (AH) are the independent predictors of mortality and/or development of complications in the history of myocardial infarction (MI) due to their stimulating influence on atherosclerosis progression. However, despite the theoretical possibilities of correction of the metabolic status in this category of patients, there are the factors which don't allow to efficiently implement this preventive mechanism in practice. In particular, this also applies to poor compliance, the peculiarities of which are understudied in patients with MS in recurrent MI.

Objective. We aimed to compare the peculiarities of metabolic syndrome correction in patients with primary and recurrent MI.

Materials and methods. The study with 5-year observation period based on the database of «Acute coronary syndrome» registry of Federal State Budgetary Scientific Institution «Research Institute for Complex Issues of Cardiovascular Diseases» («NII KPSSZ») included 421 patients who underwent a primary MI in 2009. Upon the fact of nonfatal recurrent MI development the patients are divided into two groups: 346 (73.4%) with non-complicated course of post-infarction period and 125 (26.5%) with the development of one or several recurrent MI. Initially, in the sample of patients there were the indications on the presence of T2DM in 106 (23%) patients, obesity – in 359 (76.2%), AH – in 300 (63.6%) and dyslipidemia – in 293 (62.2%). The groups were identical by the rest of clinical and anamnestic parameters. In 2015 all the patients were examined by cardiologist to assess the metabolic status, pharmacological and non-pharmacological therapy were analyzed retrospectively according to the data from case records and outpatient cards; the questionnaire survey was performed prospectively to assess the level of medical and social compliance using S.V. Davydov questionnaire. The obtained data were processed using Statistica10.0.

Results. The research has shown that the patients with recurrent MI have a poor compliance towards the correction of MS components, which is confirmed by a low integral adherence indicator as compared to the group of primary MI, 4.3+1.7 and 4.9+1.2 points correspondingly.

As regards the pharmacological and non-pharmacological correction of MS components the patients with recurrent MI less often took antihypertensive agents ($p=0.0028$) and statins ($p=0.0002$), whereas in a larger percentage of cases they use hypoglycemic agents ($p=0.0017$) and also they have hypodynamia 2 times more often ($p=0.0000$). Poor compliance is reflected in the actual indicators of metabolic profile in 2015: the patients with primary MI statistically more often achieve the normal ranges of lipid profile 43%, body weight loss 40%, targeted BP 66% ($p=0.0034$), while in recurrent MI the normalization of lipid profile was only in 30%, body weight loss 22%, BP 54% ($p=0.0439$). As for normoglycemia achievement no reliable data were obtained in both groups.

Conclusions. In recurrent MI the adherence to the implementation of the recommendations on metabolic syndrome correction is poorer as compared to the patients with non-complicated course of post-infarction period, therefore, it requires the intensification of group and individual medical and preventive work of multidisciplinary teams: cardiologists, endocrinologists, physicians, physical therapists, psychologists and dietitians.

ADIPOSE TISSUE MACROPHAGES, PROINFLAMMATORY CYTOKINES AND INSULIN RESISTANCE IN PATIENTS WITH ABDOMINAL OBESITY

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Study objectives. Abdominal adipose tissue produces a large number of macrophages and proinflammatory cytokines. We evaluated the number of adipose tissue macrophages (ATM) and level of proinflammatory cytokines in patients with IR and abdominal obesity (AO).

Material and methods. We examined 51 patients with AO (IDF, 2005) – 41 females and 9 males, 44.5±1.0 years old. Visceral fat was received from gastrocolic omentum during laparoscopic cholecystectomy in non-acute period of gall-stone disease. CD80+ (M1 macrophages) and CD163+ (M2 macrophages) cells were identified in visceral fat by fluorescence immunohistochemistry. Insulin level was measured by immune-enzyme method, levels of TNF- α and IL-6 – by ELISA. Insulin resistance level was assumed by HOMA-IR.

Results. The number of CD80+ cells and CD163+ cells in visceral fat samples didn't differ (CD80+: 47.3±2.7% and CD163+: 52.7±2.0%, $p>0.05$). Glucose level was 5.7±1.5 mmol/l, level of insulin – 19.2±2.0 mMU/ml, HOMA-IR – 4.7±0.4. Levels of TNF- α and IL-6 were 29.4 ±1.4 pg/ml and 1.6±0.2 pg/ml. We revealed correlation between CD163+ cells and HOMA-IR ($r=0.3$; $p=0.04$), CD163+ cells and insulin level ($r=0.3$; $p=0.04$), CD163+ cells and IL-6 level ($r=0.3$; $p=0.04$). We didn't found correlations between CD80+ cells and HOMA-IR, proinflammatory cytokines levels.

Conclusion. We found correlation between M2 macrophage (CD163+ cells) and HOMA-IR, level of IL-6, and we proposed that M2 abdominal adipose tissue macrophages associates with insulin resistance and IL-6 level in patients with abdominal obesity.

ANALYSIS OF RISK FACTORS AND CHARACTERISTICS OF GENETIC PREDISPOSITION AND CLINICAL- ANGIOGRAPHIC MANIFESTATIONS OF ATHEROSCLEROSIS IN PATIENT WITH ISCHEMIC ORGAN DAMAGE WITHOUT STENOTIC VASCULAR DAMAGE

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Relevance. Heart and brain are interrelated target organs of vascular pathology, clinical variants which (ischemic heart disease, stroke) continue to lead in structure of death causes in developed countries. It is known that approximately 10-20% of patients undergoing diagnostic coronary angiography due to acute or chronic ischemic syndrome, arteries are intact.

Scientific novelty. We will summarizes risk factors, clinical and angiographic, genetic testing in patients with myocardial infarction or ischemic stroke, but no signs of atherosclerotic vascular damage. Genetic testing involves identifying the examined genetic polymorphisms of the following genes: lipid metabolism; structure and tone of the vascular wall; platelet coagulation and hemostasis; inflammation, histone deacetylase, CRP, VEGFR (epidermal growth factor receptor).

Materials and methods. Pool for inclusion in the study was defined as all patients who have suffered myocardial infarction or stroke, under the supervision of the Hospital № 40 at the age of 20-59 years. The control group consists of healthy or practically healthy people. Each patient in the study start up map of the test, including the results of lipid profile with detailed indicators of coagulation, glycemic profile; ECG evaluation of possible focal changes, signs of coronary heart disease, echocardiography assessment of contractile ability of hypo-akinesia and

ejection fraction, stress tests or Holter monitoring, ultrasound of cerebral arteries, the arteries of the lower limbs, measuring ankle-brachial index, coronary angiography and study of polymorphisms of genes predisposing to the development of coronary artery atherosclerosis and cerebral arteries.

Results. Mean age was studied contingent 55; 47 women (31%), 113 men (69%); 101 of which have a history of coronary artery disease (67%), and 17 (11%) revealed stroke, repeated history of myocardial infarction had 9 people. Operations on the coronary arteries in 52 (35%) patients. The total duration of CHD was on average 1.2 years. Risk factors: smoking 88 (59%) patients, 43 (29%) patients with obesity according to BMI calculation. Dyslipidemia is revealed in the evaluation lipid 46 (31%), 89% have a history of hypertension, 77 (51%) diabetes. In assessing lipid: average total cholesterol level was 5.2 mmol/l, LDL 3.15 mol / l, TG 1.81 mmol/l. Preliminary data suggest that there is a group of patients studied genotype and phenotype features in generalized atherosclerosis without evidence of stenosis, and identify a correlation between the severity of clinical manifestations and the degree of arterial injury with existing risk factors and structural features of DNA. The results will clarify the pathogenesis of fatal cardiovascular complications in patients regardless of the presence of atherosclerotic lesion.

ANTIBIOTIC SUSCEPTIBILITY OF URINAL TRACT INFECTION PATHOGENES IN POSTMENOPAUSAL WOMEN WITH DIABETES 2 TYPES

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Revelance: The prevalence of urinary tract infection (UTI) in Russia is about 1000 cases per 100,000 population per year. [Loran O.B. Epidemiological aspects of urinary tract infections. Materials of the International Symposium «Urinary Tract Infections in Outpatients». Moscow, Russia, 1999: pp. 5-8.]. E. coli is by far the most common cause of UTIs. The most active antibiotics for E. Coli in patients with diabetes is Amoxicillinгъ/ Clavulanate (92%), Cephalosporins III-IV generations, Amikacinum (100%), fluoroquinolones (96%) [Khaikina EV, Reshedko G.K.1, Krechikova OI – Features of etiology and sensitivity to antibiotics of pathogens of urinary tract infections in patients with diabetes mellitus. Antibiotics and chemotherapy Tom: 51 Number: 3-4 Year: 2006 Pages: 13-18. Publishing house OKI ISSN: 0235-2990]. In the available literature there is insufficient data on the susceptibility to antibiotics of other pathogens of UTI in postmenopausal women with type 2 diabetes mellitus.

The purpose of the research was to study the sensitivity of the main pathogens of UTI in postmenopausal women with type 2 diabetes to main antibiotics.

Materials and methods: A retrospective analysis of the medical cards of 100 postmenopausal women hospitalized at the Railway clinical hospital at Chelyabinsk station was conducted. 57 patients (median age 68 + 8,15 years), suffering from type 2 diabetes, were treated in the endocrinology department (group I). 43 patients (median age 67.5 + 11.6 years) without diabetes mellitus were treated in the nephrologic department (group II). Both groups are comparable in age: $p > 0,05$. All patients were examined according to medical and economic standards. The statistical analysis was carried out using the BIOSTAT program, the $\chi 2$ criterion was used to compare the data.

Results of the study: according to bacteriological culture E. coli was detected in 22 patients in group I and in 14 patients in group II. E. Coli was sensitive to Nitrofurantoinum in 20 (90,91%) cases in group I and 12 (85,71%) cases in group II ($p > 0,05$). Sensitivity to Amikacinum: I group: 19 (86,36%), II group: 13 (92,86%), $p > 0,05$. Sensitivity to Cefotaxime: Group I – 19 (86,36%), Group II – 14 (100,00%), $p > 0.05$. Amoxicillinum/clavulanate was active against 18 (81,82%) pathogens in group I and 6 (81,82%) pathogens in group II, $p < 0,05$. Sensitivity to Norfloxacinum: 14 (63,64%) cases in group I, 7 cases (50,00%) in group II, $p > 0,05$.

Staphylococcus spp. They were found in 17 patients in group I and in 15 patients in group II. In the first group, oxacillinum sensitive staphylococcus were founded in 15 cases (88,24%), in group II – in 12 cases (80%), $p > 0,05$.

Among all pathogens of UTI sensitivity to amoxicillinum/clavulanate: in the I group in 38 (76%) cases, in the II group 30 (65,22%) cases, $p > 0,05$. Other antibiotics had activity in less than 50% of the cases in both groups.

Thus, the most active against E. coli in postmenopausal women with type 2 diabetes mellitus were: Nitrofurantoinum, Amikacinum, Cefotaxime and Amoxicillinum/clavulanate, which does not correspond to the literature data.

Staphylococcus spp. Were sensitive to Oxacillinum in most cases.

The widest spectrum of action was possessed by Amoxicillinum / clavulanate.

The results of the research require further study of the choice of an antimicrobial drug in the treatment of UTI in postmenopausal women with type 2 diabetes in our region

ANTIBODIES TO MODIFIED LOW DENSITY LIPOPROTEINS AND THEIR COMPLEXES: COMMUNICATION WITH CLINICAL MANIFESTATIONS OF ATHEROSCLEROSIS

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The autoimmune theory of the pathogenesis of atherosclerosis is based on the antigenicity of apo B-100-containing lipoproteins exposed to various chemical modifications. Thus, the study of involvement of anti-lipoprotein antibodies and their complexes in atherogenesis is important for formation of approaches to treatment, prevention, and possibly diagnostics of atherosclerosis.

The aim of the work was to determine the level of antibodies to a modified low density lipoprotein (LDL) and concentration Cholesterol in Circulating Immune Complexes (CIC-Chol) in blood of patients with various clinical manifestations of atherosclerosis.

253 individuals, who gave informed consent to participate in this study, were examined. The first group included of healthy individuals (n = 59); the second – 25 patients with preclinical atherosclerosis (the presence of atherosclerotic plaques in the carotid and femoral arteries was found during ultrasound investigation) and the third group included 169 patients with coronary artery disease (CAD). Key lipid parameters (total cholesterol, LDL cholesterol, high density lipoproteins (HLD), triglycerides) were determined in all subjects.

The level of antibodies (IgG and IgM classes) to LDL, modified by malondialdehyde (MDA) or acetic anhydride (acetyl) either hypochlorite was determined by the enzyme-linked immunosorbent assay (ELISA). CIC were isolated by precipitation in polyethylene glycol and then cholesterol content was determined by means of an enzymatic kit for colorimetric cholesterol determination according to manufacturer recommended protocol. Parameters were characterized by nonparametric distribution, correlation analysis was carried out using Spearman rank coefficient. For pairwise comparisons the Mann–Whitney test was used.

It was shown that in CAD patients concentration of serum CIC-Chol was significantly higher

($p < 0.0001$) however the level of IgG antibodies to all modifications was significantly lower than in healthy individuals ($p<0.001$) and patients with preclinical atherosclerosis ($p<0.01$). At the same time, there was an increase in the level of IgM antibodies to acetyl-LDL ($p<0.00001$) and a decrease to hypochlorite-LDL ($p=0.001$) in CAD patients. There were no differences in levels of antibodies and concentration of CIC-Chol between healthy individuals and patients with preclinical atherosclerosis.

Concentration of CIC-Chol correlate with antibodies IgG class to MDA-LDL ($r = -0.2$, $p<0.05$), to hypochlorite-LDL ($r = -0.28$, $p<0.05$), to acetyl-LDL ($r= -0.41$, $p<0.05$) and antibodies IgM class to acetyl-LDL ($r = 0.33$, $p<0.05$). A correlation was found between contents of IgG antibodies to MDA-LDL both to hypochlorite-LDL ($r = 0.4$, $p<0.05$) and to acetyl-LDL ($r= 0.34$, $p<0.05$).

Existence of a positive correlation between the levels of antibodies to various modifications of LDL suggests multiple modification of LDL. Nevertheless, relationship between antibodies levels and atherosclerosis presence or severity is not clear and requires further studies. On the contrary, the differences in CIC-Chol concentrations found in the groups of examined patients suggest that CIC-Chol can serve as a marker of CAD.

ANTI-REMODELING EFFICIENCY OF PREPARATIONS SUCH AS PERINDOPRIL, VEROSHPIRON AND BISOPROL APPLIED TO PATIENTS WITH CRONIC HEART FAILURE AND METABOLIC SYNDROME

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The aim of this work is to study the anti-remodeling efficiency of complex pharmacotherapy of chronic heart failure by use of perindopril, veroshpiron and bisoprolol in patients with metabolic syndrome.

Material and Methods: The study involved 76 male patients with chronic heart failure II-III functional class, with postinfarction cardiosclerosis. Prescription of myocardial infarction from 6 months to 5 years. Verification of the diagnosis carried out on the basis of the classification of the New York Heart Association (NYHA), Depending on the components of MS the patients were divided into 3 groups: Ist group (n=27), patients without metabolic syndrome; Group II (n=24), patients with a combination of dyslipidemia with abdominal obesity and hypertension; Group III (n=25), patients with a combination of abdominal obesity, arterial hypertension and dyslipidemia with diabetes of 2 types. While diagnosingthe metabolic syndrome, the diagnostic criteria of metabolic syndrome International Diabetes Federation (IDF, 2009) was used. Echocardiography was carried out on the machine Mindray (China) by method of lyingin prone position and the left side of M and B modes in accordance with the requirements of the American Association of Echocardiography (ASE). The mass of the myocardium left ventricular was calculated by the formula Devereux RB.

The results: After 3 months of treatment with Perindopril, Bisoprolol and Veroshpiron applied to patients with chronic heart failure, the data obtained shows a significant positive trend by indicators of echocardiography in patients without metabolic syndrome. The weak dynamics of the analyzed indicators was identified in patients with metabolic syndrome, especially of the third group. Despite the positive developments and progress in ultimate-systolic and ultimate-diastolic pressure and size of the left ventricle in patients of the 1st and 2nd groups, which showed statistical veracity. Three-month treatment in 1st ($p<0.01$) and 2nd, 3rd ($p<0.05$) groups contributed to the reduction of mass of the myocardium left ventricular ($p<0.01$). However, even if the data of the 2nd and 3rd groups approached each other and become nearly similar after the treatment, the indicators in the third group still remain significantly higher ($p<0.01$). A similar pattern also appears according to mass of the myocardium left ventricular. As a result of the above-mentioned structural changes in patients without metabolic syndrome, a significant improvement of systolic function is observed after the treatment showed, which is evidenced by the increase of ejection fraction ($p<0.01$). The increase of this indicator is also observed in the 2nd and 3rd groups, which did not reach statistical veracity, and lags behind by 8.3% ($p<0.05$) and 21% ($p<0.01$) respectively, compared to the 1st group.

Conclusions: A three-month treatment with an implement of the Perindopril, Bisoprolol and Veroshpiron combination in patients suffering from chronic heart failure without metabolic syndrome promotes regression of non-adaptive remodeling of myocardial and improvement of systolic and diastolic function of the heart.

APOLIPOPROTEIN B/APOLIPOPROTEIN A1 RATIO AS A PREDICTIVE MARKER OF METABOLIC SYNDROME

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Background: It has been demonstrated that an increased apolipoprotein B/apolipoprotein A1 ratio (ApoB/ApoA1) is associated with atherogenic low density lipoprotein (LDL) particles and the development of clinical cardiovascular disease.

Purpose: to estimate relation between apolipoprotein B/apolipoprotein A1 ratio (ApoB/ApoA1) and metabolic syndrome (MS) risk in organized Russian population.

Methods: 500 community residents were enrolled: 347 females (69%), age 41,8±0,4 years and 153 males (31%), age 44,6±0,3 years. MS was diagnosed according to International Diabetes Federation criteria (2005). Office blood pressure (BP) was measured by Korotkov method, medical history was also analyzed. Fasting leptin, insulin, glucose, lipid profile including ApoB and ApoA1 were measured. Statistical analyses were performed with SPSS 20.0 for Windows.

Results: Abdominal obesity (AO) was determined in 70% of responders, 52% were hypertensive, hypertriglyceridemia was observed in 32%, 68% had serum high density lipoproteins level (HDLP) decreased and hyperglycemia was diagnosed in 51% responders. 40% of examined people had two or more components of MS. The ApoB/ApoA1 ratio was significantly higher in subjects with MS, compared to those who had not MS (1,38±0,03 vs 0,62±0,01; p=0,001). The ApoB/ApoA1 ratio was the highest in the cohort of patients with four or more components of MS – 1,53±0,03. The ApoB/ApoA1 ratio in those who had three components of MS was 1,32±0,02; in those who had two components of MS was 1,05±0,04 (p= 0,01).

We revealed significant positive correlations between high ApoB/ApoA1 and leptin, insulin, low density lipoprotein (LDLP) level and systolic BP (r=0,21; 0,236; 0,599 and 0,152 accordingly; p=0,0001). Significant negative correlations were revealed between high ApoB/ApoA1 and adiponectin and HDLP (r= -0,228 and -0,517; p=0,005 and 0,0001 accordingly).

Conclusion: High ApoB/ApoA1 ratio is associated with metabolic syndrome and with cardiovascular and metabolic factors determined to this syndrome in organized Russian population.

ASSOCIATIONS BETWEEN +45T>G GENOTYPE WITH LEVELS OF TOTAL AND HIGH MOLECULAR WEIGHT ADIPONECTIN AND RISK OF METABOLIC SYNDROME IN PATIENTS WITH ABDOMINAL OBESITY

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BACKGROUND: Adiponectin is a protective adipocytokine in humans. Low levels of adiponectin in persons with abdominal obesity are associated with the metabolic syndrome, endocrine and cardiovascular diseases. Adiponectin is the most abundant fatty protein; it circulates in plasma in various isoforms. Many researchers discuss the biological significance of various isoforms of adiponectin. Studies show that the G45T association polymorphism of the adiponectin gene with various adiponectin isoforms and the development of metabolic syndrome differs in different populations. However, the results of these studies have proven to be inconsistent. We hypothesized that the G45T gene for adiponectin polymorphism may be associated with certain adiponectin isoforms and the risk of metabolic syndrome.

METHODS: We examined 328 patients (285 women and 43 men) with abdominal obesity (AO) (IDF, 2005) and 187 controls at the age of 30-55 years. The metabolic syndrome (MS) was 55,2% (women (n = 156), men (n=25)), (IDF, 2005). We determined the levels of high molecular weight adiponectin (HMWA) and total adiponectin (TA) using BioVendor assays. The T45G polymorphism was identified by PCR and restriction analysis.

RESULT: TA and HMWA in women without MS were higher than in women with MS: for TA [21.32 (2.55, 45.32) mcg.ml and 18.17 (1.6, 52.26) mcg.ml, respectively; P = 0.038], for HMWA [3.04 (1.55, 15.45) mcg.ml and 2.27 (0.5, 8.24) mcg.ml, respectively; P = 0.001]. HMWA was the only isoform of adiponectin that affected the risk of MS (logistic regression analysis (p = 0.001). TA and HMW levels didn't different in men with and without MS (p>0,05).

The T45G genotype was identified in 71 patients and T45T genotype – in 257 patients. Results show that women with the T45T genotype (n=220) have a lower level of HMWA (but not TA) than those with genotype T45G (n=65) [2.30 (0.5, 8.24) and 3.58 (1.08, 15.45), respectively, p <0,01].

We found that women with the T45T genotype have a higher risk of MS than women with the G45T genotype. T45T against T45G: OR = 2.5 95% CI (1.29-4.85). There were no associations of T45G polymorphisms with TA, HMW, and MS in men with AO (p> 0.05).

CONCLUSION: The T45T genotype of the adiponectin gene in women with abdominal obesity may be a risk factor for metabolic syndrome due to its associations with lower levels of high molecular weight adiponectin, but not total adiponectin.

ATRIAL FIBROSIS, EPICARDIAL FAT IN PATIENTS WITH A LONE ATRIAL FIBRILLATION

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Introduction and objectives: Visceral adipose tissue has proinflammatory and profibrogenic effects and increase risk of atrial fibrillation (AF). Epicardial fat is localized near myocardium and may stimulate remodeling of the heart. Voltage changes mapping allows to investigate left atrium electrical remodeling. The aim of the study was to reveal possible connection between left atrium fibrosis degree and epicardial fat thickness (EFT).

Materials and methods: 25 patients with paroxysmal symptomatic AF 58,54±4,18 years old (14 males, 11 females) were included in study. AF duration was 3,83±1,99 years. The epicardial fat thickness (EFT) was measured by transthoracic echocardiography over free wall of right ventricle. Ablation procedure was performed with the system of electroanatomical mapping CARTO 3 (Biosense Webster Inc, USA) and contact force monitoring catheter (SmartTouch). Left atrium anatomical and amplitude maps were created with contact force parameters 3 to 40 g / cm^2 (more than 300 points). After mapping and pulmonary vein antrum verification isolation of pulmonary veins was performed (30-40 watts) up to complete disappearance of electrical activity.

Results: Epicardial fat thickness in AF patients was 5,54±1,98 mm. Waist circumference was 96,0±14,2 cm. Left atrium volume (LAV) in AF patients was 81,3±29,8 cm and LAV index was 40,7±12,2 cm/m^2. A positive correlation between epicardial fat thickness and LA fibrosis degree was revealed (r=0,623; p=0,001). There was not established significant correlation between waist circumference and LA fibrosis degree (p=0,681).

Conclusions: Left atrium fibrosis degree correlates with epicardial fat thickness, but left atrium fibrosis degree is independent from waist circumference. We can suppose that epicardial fat thickness (measured by ultrasound method) is a significant prognostic factor for atrial fibrillation recurrence.

CHARACTERISTICS OF THE DAILY DIET IN PATIENTS WITH METABOLIC SYNDROME WITH AND WITHOUT GALLSTONES

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Aim. Investigate the product set the daily diet (DD) in patients with metabolic syndrome (MS), with and without gallstones (GS).

Materials and methods. MS criteria meet the requirements of NCEP (ATP-III, 2001), GS diagnosed by sonography. The actual nutrition in the open one-stage clinical trial on «case series» type has been studied in 47 patients with MS (30 patients with GS and 17 – without GS) using a validated frequency questionnaire, including 142 products in the last 3 months. In a specially constructed mathema-tical model (developed by Verevkin E.G.) product set the DD was calculated.

Results. As fat and carbohydrate DD components in all MS patients is unbalanced: the proportion of the total intake of fat – 43,2%, total carbohydrates – 42,3%, total protein – 14,5% of DD energy. Daily intake of fat in MS patients with and without GS were significantly higher than normal, and in both groups of MS patients predominate animal fats (172±73 and 102±65 g/day, $p<0,05$), compared with the vegetable fats (11±5 and 6±3 g/day, $p>0,05$, the norm of 20-25 g/day). The consumption of meat products increased in MS patients with and without GS (208±101 and 173±84 g/day, $p> 0,05$, the norm of 100 g/day), the consumption of fish and fish products, on the contrary, decreased (57±36 and 65±41 g/day, $p>0,05$, standard 70 g/day). In MS patients with and without GS vegetable consumption is reduced (423±81 and 299±70 g/day, $p<0,05$), fresh fruit and berries (292 ±94 and 91±37 g/day, respectively, $p<0,05$), norm of 500 and 300 g/day, respectively. The consumption of juices and beverages drastically reduced in both groups of MS patients (65±24 and 51±26 g/day, $p>0,05$, the norm of 200-300 g/day), and the consumption of simple carbohydrates – sugar and confectionery products – increased as in MS patients with and without GS (133±87 and 159±95 g/day, $p>0,05$, norm of 50 g/day).

Conclusions. DD in MS patients imbalanced – dominated by fat and not enough carbohydrates, protein component is correct. In product set consumption of meat products and simple carbohydrates dominates in MS patients, the consumption of vegetable fats, fruits and vegetables notably below the recommended values, although MS patients and GS consumed significantly more vegetables, fresh fruit and berries, than MS patients without GS.

CYTOKINES IL-1BETA, TNF-ALPHA GENE POLYMORPHISMS AND THEIR PROTEIN PRODUCTS IN WOMEN WITH METABOLIC SYNDROME AND GALLSTONE DISEASE

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Aim: To evaluate gene polymorphism of the cytokines IL-1β and TNF-α and the IL-1β and TNF-α levels in the blood serum in women with metabolic syndrome (MS) in combination with Gallstone Disease (GSD).

Materials and Methods: We investigated 97 women: 67 patients with MS and GSD (1st group) and 2nd group – 30 patients with GSD without MS. МС использована классификация NCEP ATP III (2004 г.). For MS classification criteria used by NCEP ATP III (2004). Gene polymorphism IL-1β (rs16944, –511T>C) and TNF-α (rs1800629, -308G>A) was examined by PCR. IL-1β and TNF-α levels were determined by standard methods. Statistical analysis was performed by SPSS (13.0).

Results: in 1st group we found no significant differences when compared average TNF-α serum levels between carriers of G-allele (4,6±0,51 pg/ml) and A-allele (4,91±0,73 pg/ml) and IL-1β levels in carriers of C-allele (0,42±0,07 pg/ml) and T-allele (0,48±0,12 pg/ml) of corresponding genes. Similar results were obtained in the 2nd group when comparing the cytokine levels: TNF-α levels in G-allele (1,31±0,21 pg/ml) and in A-allele (1,19±0,33 pg/ml), IL-1β levels in C-allele (0,41±0,15 pg/ml) and in T-allele (0,36±0,16 pg/ml, $p>0,05$ in all cases). In the 1st group in carriers of both alleles G and A TNF-α levels were significantly higher than in 2nd group both in G-allele ($p<0,001$) and A-allele ($p<0,001$). IL-1β levels did not differ between two groups ($p>0,05$).

Conclusion: serum TNF-α levels in the 1st group patients with MS and GSD were much higher than those in the 2nd group ($p<0.001$), but serum TNF-α and IL-1β levels were independent of the corresponding gene polymorphisms in the two groups.

COMMON POLYMORPHISMS AS STRONG PREDICTORS OF HYPERTRIGLYCERIDEMIA IN CZECH POPULATION

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Aim: Hypertriglyceridemia (HTG) is a common lipid disorder. It is supposed, that really high plasma levels of triglycerides (over 10 mmol/L) have strong genetic background. Rare mutations within the genes for LPL, APOA5, APOC2, GPIHBP1 and LMF1 explain some cases, but in majority of the patients, the disease seems to be polygenic. Accumulation of risky alleles can nonlinearly increase the risk of HTG.

Methods: Using PCR-RFLP we have analysed common polymorphisms within the genes *APOA5* (rs96484), *FRMD5* (rs2929282), *GCKR* (rs1260326), *CAPN3* (rs2412710) and *TRIB1* (rs2954029) in 145 patients with plasma TG values over 10 mmol/L and 515 control subjects with plasma TG below 1.8 mmol/L.

Results: In all cases, we have found highly significant risk (all $P < 0.01$) of hypertriglyceridemia development associated with the minor alleles of the above mentioned SNPs. The risky alleles increased the risk (OR, 95%CI) of HTG for 1.62 (1.09-2.40; *TRIB1*), 2.74 (1.19-6.33; *CAPN3*), 2.56 (1.64-4.00; *GCKR*) and 2.05 (1.19-3.53; *FRMD5*). The extreme association has been observed in the case of the *APOA5* gene, where the GG homozygotes exhibit more than 15-times higher risk to develop HTG (OR 15.16, 95%CI 6.40-36.04; $P < 0.000001$). The mean of the risky alleles per person was 1.03 in HTG group vs. 0.48 in controls ($P < 0.01$).

Conclusions: Our results clearly confirm that the common SNPs in distinct genes are strong predictors of the HTG development.

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COMPLIANCE WITH THE TREATMENT OF PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Compliance is understood as the degree of compliance of the patient's behavior with the recommendations received from the doctor regarding the intake of medications, compliance with diet and other measures of lifestyle change.

Background and aims: to assess the compliance to the treatment of patients with type 2 diabetes mellitus (DM).

Materials and methods: 92 patients (30 men and 62 women) were examined with type 2 diabetes. The average age of the patients was 59.3 ± 2.4 years. The duration of the disease is 8.8 ± 1.8 years. The average level of HbA1c is 8.1 ± 0.8%. Patients received the following treatment: tablets – 49.5%, insulin – 20.8%, combination (tablets + insulin) – 29.7%. Adherence to the treatment of patients with diabetes was assessed using questionnaires developed in the framework of this study and the generally accepted standardized Russian-language questionnaire Morisky-Green. Statistical processing was carried out in the program Statistica 7.0

Results. According to the questionnaire, 60.4% of patients did not follow the doctor's recommendations. The most frequent reasons for this were: forgetfulness (47.3%), difficulty in taking medications (24.2%), high cost of treatment (23.1%), and other causes (37.4%), such as: poor awareness of the disease, lack of contact with a doctor, disbelief in the success of treatment and the need to make injections. According to the questionnaire, the control of the sugar level is carried out: 1-2 times a month – 15.4%, 1-3 times a week – 19.8%, once a day – 16.5%, more than once a day – 45%, do not conduct glycemic control – 2.2% and 1.1% do not have a glucometer. Positive correlations were found between the average costs of one patient per month (2283 ± 371 rubles) with the degree

of compensation for diabetes; Between the evaluation of the quality of care and strict compliance with the recommendations of the physician by patients ($r = 0.563$ and $r = 0.614$, respectively, $p < 0.05$).

Conclusion. 1. The main part of the questioned patients noted a low adherence to treatment due to the high cost of hypoglycemic drugs, etc., the need for combined therapy, frequent self-management of glycemia and a visit to a doctor

2. Compliance with the treatment, first of all, is determined by the motivation and readiness of patients to obtain new data on the disease and its complications, as well as the possibility of modern treatment.

CONTRIBUTION OF IMPROVEMENT OF THE HYPOTHALAMIC SIGNALING TO THERAPEUTIC EFFECTS OF METFORMIN IN OBESITY

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Metformin (MF), a biguanide derivate, is commonly used for treating metabolic syndrome and type 2 diabetes mellitus (T2DM). The MF therapy improves insulin sensitivity and energy metabolism in the periphery. There is evidence that these effects can be realized due to the influence of MF on functional activity of hypothalamic neurons. At the same time the central effects of MF are still poorly understood. The objective was to study MF effects on functional activity of peptidergic and monoaminergic signaling systems, AMP-activated kinase (AMPK), and the proteins involved in the regulation of apoptosis and mitochondrial dynamics in hypothalamic neurons of agouti mice (Ay/a) with the melanocortin type obesity.

The C57Bl/6J mice were taken as control. The treatment of agouti-mice with MF during 9 days at a daily dose 200 mg/kg led to the decrease of the body and fat weight and to the improvement of glucose tolerance, insulin sensitivity and lipid metabolism. Alongside with the metabolic effects, MF treatment of agouti mice led to restoration of the expression of Mfn1 and Drp1 proteins participating in regulation of mitochondrial dynamics in hypothalamic neurons and to normalization of the expression of pro-opiomelanocortin, a precursor of anorexigenic melanocortins. It also improved the functional activity of hypothalamic leptin signaling system, which was illustrated by increase of Ser^{473}-phosphorylation of Akt-kinase in MF-treated agouti mice. The treatment of agouti mice with MF did not change the stimulating Thr^{172}-phosphorylation, but decreased the inhibiting $Ser^{485/491}$-phosphorylation of hypothalamic α2-subunit of AMPK, resulting in the increase of hormone-stimulated enzyme activity. In agouti mice the activity of the Bax and Bcl-2 proteins that regulate the apoptotic processes in hypothalamic neurons did not differ significantly from C57Bl/6J mice, and MF had a little effect on these proteins. The mRNA and protein expression of type 1 dopamine receptor (D1-DR) was reduced in MF-treated animals, while the expression of D2-DR did not change, and, as a result, the ratio of D1-DR and D2-DR was decreased, indicating the enhancement of D2-DR signaling pathway in the hypothalamus of agouti mice. We concluded that the long-term treatment of obese agouti mice with MF restores mitochondrial biogenesis in the hypothalamic neurons and improved the leptin and dopamine signaling pathways in them, which contributes to MF-induced improvement of metabolic processes in the periphery.

This work was supported by Russian Science Foundation (No 16-15-10388).

DEFEAT OF ANTERIOR DESCENDING ARTERY AND ITS EFFECT ON THE CONTRACTILE FUNCTION OF THE LEFT VENTRICLE IN PATIENTS WITH ISCHEMIC HEART DISEASE IN COMBINATION WITH A DIABETES MELLITUS OF TYPE 2

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Objective: To assess the interdependence of atherosclerotic lesion of the anterior descending artery (ADA) and systolic function of the left ventricular (LV) in patients with coronary heart disease (CHD) in combination with type 2 diabetes mellitus.

Material and methods: 33 patients were examined (the mean age was 58.7 ± 9.4 years), from which 5 (15.2%) were women. All the studies were carried out: examination, history taking, laboratory tests, ECG, echocardiography with measurement of the ejection fraction (LVEF) and coronaroangiography (CAG) followed by stenting of the ADA. Differences were considered valid for $p < 0.05$.

Results: The average blood glucose level in the whole group was 8.3 ± 2.5 mmol / l. The average caliber of the PNA = 3.39 ± 0.35 mm. The average percentage of stenosis ADA = 89.25 ± 8.79%. Isolated lesion of the proximal part of the ADA occurred in 19 (57.6%) cases; the middle part – in 7 (21.2%); combined lesion of the proximal and middle parts was detected in 6 (18.2%) patients and in 1 (3%) patients there was a combination of lesions of the proximal and distal parts of the ADA. The study showed a distinct prevalence of stenosis complex type in this category of patients: the types B and C were observed in 9 (27.3%) and 23 (69.7%) cases. Mean LVEF = 56.5 ± 7.9%, and 5 (15.2%) patients having LVEF <50%. An inverse correlation was established between the caliber of ADA and LVEF ($p = 0.009$, $r = 0.196$, $t = -2.757$) от the one hand, and between the level of stenosis and LVEF ($p = 0.065$; $r = 0.105$; $t = -1.906$) on the other.

Conclusion: The presence of type 2 diabetes contributes to aggravation of angiographic lesions in the ADA basin characterized predominantly by proximal localization and prevalence of C-type stenosis, which is accompanied by a decrease in the systolic function of the myocardium of left ventricular ($p < 0.05$).

DYNAMICS OF METABOLIC HEALTH IN PERSONS WITH METABOLICALLY HEALTHY OBESITY

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Purpose: To study the prevalence of «metabolically healthy obesity» and its dynamics during 3-year prospective follow-up in a population sample aged 45–69 years old.

Materials and Methods: A random population sample of men and women aged 45-69 years old was examined in Novosibirsk in 2003-2005 (baseline survey, project HAPIEE). In a prospective study, 3195 individuals were examined in the first survey (2003-2005) and re-examined in repeated survey (2006-2008). Those with obesity and two or less components of the metabolic syndrome (MS; NCEP ATP III criteria), were included for analysis n=491. The average duration of prospective follow-up complied of 3±0,01 years. Anthropometric measurements, biochemical assessment of lipid and glucose levels were performed.

Results: According to the baseline data from screening of 2003-2005, the prevalence of metabolically healthy obesity in persons of both sexes was 15%, n=491 (8% men, n=100; 20% women, n=391, p<0,001). Among those examined twice, the metabolic syndrome was developed in 20%, n=96; BMI reduction to <30 kg/m² was registered in 12%, n= 58; BMI reduction to <30 kg/m² with increased number of MetS-definitions was registered in 0,8%, n= 4. The obesity without MS preserved in the rest participants (67,8% from baseline group).

The proportions of individuals with baseline obesity and without MS who reduced their body weight in 3 years, was 18% in men and 10% in women (p<0,05). In other subgroups, significant difference between sexes was not found (p > 0,05).

Conclusions: After 3-year follow-up, obesity without MS persisted in 67.8%. The metabolic syndrome was developed in every fifth person. The reduction of body mass without development of metabolic syndrome was registered for men 1,7 times more often than for woman (p<0,05).

Key words: obesity, body mass index, dynamics, metabolic syndrome.

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DYNAMICS OF PARAMETERS OF MACRO- AND MICROCIRCULATION IN PATIENTS WITH DIABETES MELLITUS TYPE 2 AT ADMINISTRATION OF ACTOVEGIN

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The changes of vessels in microcirculatory bloodstream are one of the most important manifestations of diabetes mellitus that determines the features of the course, complications and outcomes of this disease. Changes in vessels at diabetes occur as a result of metabolic changes and the development of tissue hypoxia. The administration of drugs, which have antihypoxic and antioxidant effects (for example, Actovegin), at the earliest stages of diabetes will prevent the development of severe complications, in the pathogenesis of which hypoxia, ischemia and oxidative stress play a role.

The goal of the study is to evaluate the effect of treatment by Actovegin on the parameters of the microcirculation of the capillary bed, the rigidity of the arteries and endothelial function in patients with diabetes mellitus type 2.

Materials and methods. A comparative study of parameters of microcirculation, rigidity of the arteries and endothelial function was conducted in patients with diabetes mellitus type 2 before and after administration of Actovegin (group «A», n=20) and in patients with diabetes mellitus type 2 without administration of Actovegin (group «B», n=20).

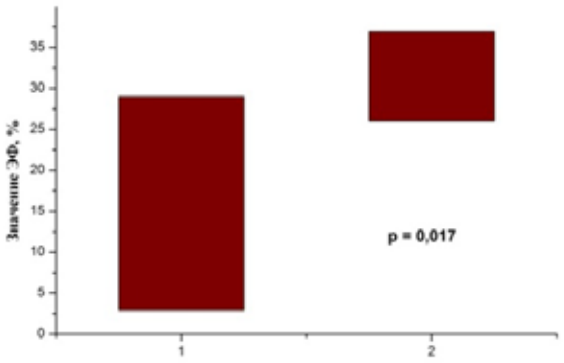
Results. The improvement of microcirculation parameters was received: the dilatation of arterial part of the capillaries at administration of Actovegin (p=0.005). In patients with an initially reduced endothelial function, a significant increase in its function (p=0.017) was observed at administration of Actovegin, as well as a reduction of perivascular edema (p=0.059) was near-significant. Treatment with Actovegin does not effect on the parameters of central hemodynamics and arterial rigidity in patients with diabetes mellitus type 2 (p=0.778).

Conclusion. The results of the conducted study clearly demonstrated that the administration of the drug with antihypoxic action (Actovegin) significantly improves the parameters of microcirculation in patients with diabetes mellitus type 2 and, therefore, can be recommended as a pathogenetic therapy at the earliest stages of diabetes.

Table 1. General characteristics of study subjects.

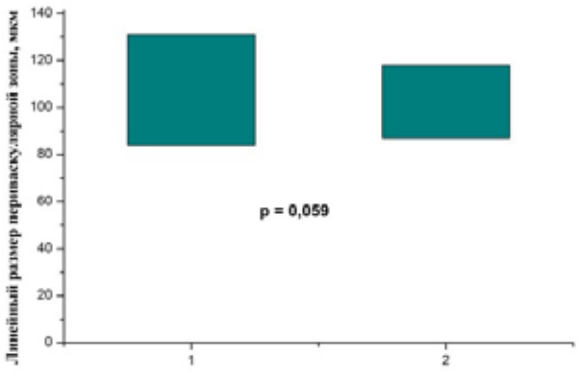
Parameters	**Group «A» before treatment (n=20)**	**Group «B» Initial (n=20)**	P
Gender, m*/f, %*	15/85	25/75	0,489
Age, *years*	58 (54; 62)	54 (52; 60)	0,347
Duration of DM, *years*	1 (0; 5)	4 (2; 5)	0,092
Duration of AH, *years*	6 (3; 10)	10 (8;12)	0,428
BMI, *kg/m²*	34,2 (31; 36)	32,0 (30; 34)	0,182
Glycated hemoglobin, *%*	6,4 (6,2; 7,0)	7,1 (6,7; 7,3)	0,073
Smoking, *%*	20	20	0,987
Family history of DM, *%*	40	45	0,567

Fig. 1. Dynamics of the average size of the arterial part of capillaries (AP) in patients with diabetes with an initially reduced EF before (1) and at administration of Actovegin (2).



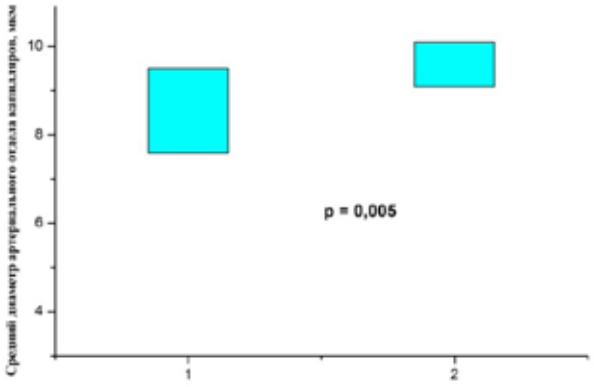
p – level of significance.
Average diameter of arterial part of capillaries, μm

Fig. 2. Dynamics of endothelial function in patients with diabetes with an initially reduced EF before (1) and at administration of Actovegin (2). p – level of significance



EF, %

Fig. 3. Dynamics of the linear size of the perivascular zone (PZ) in patients with diabetes with an initially reduced EF at before (1) and at administration of Actovegin (2). p – level of significance.



Linear size of the perivascular zone, μm

DYSLIPIDAEMIA CORRECTION IN THE THERAPY OF PATIENTS WITH METABOLIC SYNDROME AND OSTEOARTHRITIS

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Aim. To investigate the atorvastatin influence on severity of dyslipidaemia, the circadian blood pressure (BP) profile (CBPP) and articular syndrome in patients with metabolic syndrome (MS) in combination with osteoarthritis (OA).

Materials and methods. 90 patients with essential hypertention stage II in combination with OA of the knee joints I-II x-ray Kellgreen and with plasma concentration of the total cholesterol (TCH) more than 5.0 mmol/l and the cholesterol low density lipoproteins (LDL) more than 3.5 mmol/l before and after 3 month of therapy with 20-40 mg lisinopril and 20 mg atorvastatin were surveyed. There were determined CBPP, endothelial function in reactive hyperemia (RH) on the brachial artery, the degree of resorption of the bone tissue by C-terminal telopeptides determination in urine with immuno-enzyme method, calcium concentration in the serum and in the urine, the intensity of the calcium transport between the kidneys, extracellular fluid and bone tissue, the Lekena algofunctional articular index, and assessment of joint pain in the visual-analogue scale.

Results. After atorvastatin treatment the average TCH level has decreased ($p<0.05$) from 5.89±0.13 mmol/l to 4.08±0.09 mmol/l, the cholesterol LDL level – from 3.77±0.07 mmol/l to 2.10±0.09 mmol/l. The TCH level in all patients did not exceed 4.50 mmol/l. The level of LDL-C did not exceed 2.60 mmol/l. After therapy with atorvastatin systolic BP (SBP) decreased to 125.9 mm Hg, diastolic BP (DBP) – up to 76.4 mm Hg. The degree of night reduce of SBP increased to 16.7±1.7 mm Hg, DBP up to 15.1±1.5 mm Hg. The average circadian variability of SBP decreased from 14.1±0.4 mm Hg to 12.7±0.5 mm Hg. Vasodilation in the RH has increased from +8,3±0,5% ($p<0.05$) to +10.4±0.3%, the concentration of C-terminal telopeptides in the urine from 252.5±16.1 to 108.0±13.3 mg/mmol creatinine ($p<0.05$) was noted in patients. Calcium transport between the extracellular and bone sectors in patients with MS and OA (-0.047±0.007 mmol/l; $p <0.05$) is slowed down in comparison with healthy persons (-0.108±0.009 mmol/l). The intensity of the calcium transport between the extracellular fluid and bone tissue has increased almost in 2 times ($p<0.05$). Much more significant deceleration (-0.033±0.004 mmol/l; $p<0.05$) was found in individuals with a high plasma level of TC (above 6.00 mmol/l) and LDL-C (above of 3.80 mmol/l) compare to patients lower plasma level of TC (-0.051±0.005 mmol/l). It was in those patients who had the highest increase in the intensity of calcium transport up to -0.093±0.006 mmol/l

($p<0.05$) after treatment with atorvastatin. Lekena index decreased from 8.7±0.9 to 5.3±0.5 points ($p<0.05$), pain when rising – from 44.4±3.3 to 20.1±2.0 mm, pain when passing the distance of 200 m – from 39.6±3.2 to 17.7±1.4 mm.

Conclusion. Hypocholesterolemic and the stimulating effect of atorvastatin on the endothelial synthesis of nitric oxide accompanied by vasodilation, the improvement of the CBPP and clinical-functional state of the joints due to the direct effects on the joint and indirect – on subchondral bone and its blood supply. One of the mechanisms of the atorvastatin effect is the correction of calcium metabolism disorders due to its hypocalciuretic and anti-resorption impacts.

EFFICIENCY OF ATORVASTATINE USE IN PATIENTS WITH THE DIABETUS MELLITUS TYPE 2 IN COMBINATION WITH ESSENTIAL HYPERTENSION

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Aim. Assessment of the effectiveness of statin inclusion in the treatment complex of patients with diabetes mellitus (DM) type 2 in combination with essential hypertension (EH).

Objects and methods of research. The study included 60 patients (32 men and 28 women) with stage II AH (age 7.9 ± 0.8 years old) in combination with type 2 diabetes (age 4.5 ± 0.6 years) at the age of 43-77 years, the average age of patients Was 60.4 ± 1.52 years. Arterial pressure against the background of antihypertensive therapy with lisinopril at a dose of 10 mg and amlodipine 5 mg corresponded to the following indicators-142.3 ± 6.3 / 88.1 ± 1.67. The level of glycosylated hemoglobin was 8.3 ± 1.4%. Until the moment of inclusion in the study, none of the patients did not receive lipid-lowering drugs. Patients were randomized to 2 comparable by sex, age, clinical and laboratory characteristics of diabetes and the group's hypoglycemic therapy. Patients of the 1 st group (30 people) were prescribed atorvastatin at a dose of 20 mg / day for 24 weeks. From the study patients with type 2 diabetes with proteinuria more than 300 mg per day, infectious diseases of the kidneys, kidney stone disease were excluded. The concentration of albumin in the urine was examined in a portion of the daily volume of urine. The enzyme immunoassay method was used (a set of the company «ORGenTec GmbH», Germany). Microalbuminuria (MAU) was diagnosed if the albumin excretion was within the range of 30 to 300 mg / 24 hours. All patients were assessed for total cholesterol (TC) and serum creatinine on Biosystems A25 automatic biochemical analyzer using standard diagnostic kits. The glomerular filtration rate (GFR) was calculated using the standard Concroft-Gault formula. We used the package of statistical programs «Microsoft Office Excel 2013». The data are presented in the form M ± m, where M is the mean value, m is the error of the mean. Statistically significant differences were considered for $p<0.05$.

Results. In patients of the 1 st group receiving lipid-lowering therapy, there was a significant decrease in the level of total cholesterol from 5.77 ± 0.18 mmol / l to 4.96 ± 0.14 mmol / l. In the control group, the values of total cholesterol significantly did not change and amounted to 5.52 ± 0.19 mmol / l, in comparison with baseline (5.68 ± 0.22 mmol / l). MAU before the study in the 1 st group was 139.6 ± 31.16 mg / 24 hours, and in the second group-127.1 ± 24.3 mg / 24 hours. Patients treated with atorvastatin had a significant ($p<0.05$) decrease in albuminuria to 104.7 ± 31.18 mg / 24 hours. In the control group, on the contrary, the level of UIA slightly increased to 152.52 mg / 24 hours. Addition of atorvastatin for 6 months to the treatment complex was accompanied by a pronounced nephroprotective effect (decrease in the level of MAU). In the control group of patients, after 24 weeks of observation, there was a significant decrease in the level of creatinine, an increase in GFR from 83.84 ± 4.26 and 98.7 ± 4.93 to 77.63 ± 3.72 and 105.37 ± 4.88, respectively. In the 1 st group, there were similar changes in creatinine levels (81.44 ± 3.72 at the beginning and 76.23 ± 3.34 at 6 months) and GFR (98.2 ± 4.72 at the beginning and 105.8 ± 4 , 92 in 6 months). Large international studies in recent years show no effect of taking statins on GFR.

Conclusion. Addition of atorvastatin at a dose of 20 mg per day to patients with DM type 2 in combined with AH is accompanied by a nephroprotective effect manifested in a decrease in the level of MAU in the absence of

negative dynamics of creatinine and GFR levels with 10 mg of lisinopril and 5 mg of amlodipine, and a significant decrease in TC level .

EFFECT OF BODY WEIGHT ON SPONTANEOUS AND INDUCED SECRETION OF OXYGEN RADICALS BY FEMALE BLOOD PHAGOCYTES AFTER MENOPAUSE

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Oxygen radicals generated by blood phagocytes play an important role in cardiovascular diseases. With oxidative stress, they are involved in angina pectoris, injury of heart cells after ischemia-reperfusion, myocardial infarction and heart failure. The activity of blood neutrophils and monocytes entering the focus of inflammation after the death of cardiomyocytes determines the rate of modified cells remove and the restoration of the contractile function of the myocardium. In the blood, phagocytes can be in one of three states: a state of rest; pre-activation (priming) and stimulation. Different risk factors cause a transition from one state to another. Only pre-activated cells respond to stimulation by the pronounced formation of oxygen radicals. Fat cells are not only responsible for the accumulation and preservation of lipids, but also produce more than 80 biologically active agents – adipokines, which affect various types of cells, including human phagocytes.

Objective. To investigate whether weight gain is one of the risk factors that translates blood phagocytes from dormancy to priming in women after menopause with a high body mass index.

Materials and Methods. Lucigenin, phorbol ether (PMA), formyl peptide (FMLP), leptin, dimethyl sulfoxide from Sigma-Aldrich were used in the work. Peripheral blood was taken from the ulnar vein into plastic tubes with heparin (30 IU / ml). Blood samples were obtained from 12 women with a high body mass index (BMI) (58 ± 6 years, weight 82 ± 7 kg, height 162 ± 7 cm, BMI 31.5 ± 5 kg / m2) and 8 women with low BMI (59 ± 4 years, weight 63 ± 5 kg, height 164 ± 5, BMI 23.3 ± 4 kg / m2). The formation of oxygen radicals by blood phagocytes was determined from the chemiluminescence of lucigenin (30 μM) on the Biotox-7 chemiluminometer and expressed in the number of pulses per second, and was also estimated from the integral values of the luminescencese for 60 sec.

Results. In the blood of all women with high BMI, the content and activity of pre-activated (primed) phagocytes was increased, as evidenced by the «spontaneous» formation of oxygen radicals in blood samples as a result of their interaction with the walls of the cuvette. The rate of spontaneous formation of ROS over a fixed time was 3.4 times higher than the rate in blood samples of women with low BMI values. In addition, the responses of blood phagocytes in the first group to the action of standard stimulants-FMLP (2 μM) and PMA (1 μM) were significantly higher in terms of maximum amplitude and rate of formation of superoxide anions in obesity women compared to lean ones. Leptin (250 ng / ml) did not induce ROS formation, but increased after 2 hours incubation the response of blood phagocytes in three women with low BMI to subthreshold doses of PMA (5x10-8 – 10-7 M). The drug actovegin in dosa-dependent manner (from 2 to 4 mg / ml) reduces the levels of spontaneously generated oxygen radicals, as well as the levels of oxygen radicals induced by FMLP and PMA. This inhibitory effect was more pronounced in the group of women with a high BMI.

Conclusions. An increase in body weight leads to the formation of pre-activated phagocytes in the blood, responding to stimulants in a more pronounced manner, and creates the prerequisites for the formation of systemic inflammation.

EMPAGLIFLOZIN-INDUCED CARDIOPROTECTION IN METABOLIC NEUTRAL HEART FAILURE (EXPERIMENTAL STUDY)

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Background. EMPA-REG OUTCOME trial results shows that anti-diabetic drug sodium glucose cotransporter 2 (SGLT2) inhibitor empagliflozin can reduce the frequency of hospitalizations for heart failure in high risk patients with diabetes mellitus.

Purpose. We experimentally tested the hypothesis about efficacy of SGLT2 inhibitor empagliflozin in the treatment of chronic heart failure (CHF) in the absence of carbohydrate metabolism disorders.

Methods. CHF model was created in 31 rats by permanent left coronary artery ligation. All rats were divided into three groups: group 1 consisted of 11 CHF-rats treated with empagliflozin (1 mg / kg) for three months; group 2 included 11 untreated rats with CHF; and group 3 (control group) consisted of 9 sham-operated rats. Echocardiography was performed every month for all rats to evaluate left ventricular (LV) structure and function parameters, such as: LV dimensions and volumes, LV ejection fraction, LV stroke volume and cardiac output. At the end of the study treadmill test was performed for all rats to measure a maximum exercise time.

Results. Rats of group 1 had a higher cardiac output at rest (80±30.1 ml / min vs. 57±19.4 ml / min, $p<0.025$), greater end-diastolic volume (0.50±0.14 ml vs. 0.39±0.08, $p=0.028$), and greater LV mass (1.09±0.19 g vs. 0.69±0.10 g, $p=0.012$) than untreated rats of group 2.Maximum treadmill exercise time was longer in rats treated with empagliflozin than in untreated rats (900sec ±110 sec vs. 645sec±110 sec, $p=0.0004$). An increasing of LV stroke volume, end-diastolic volume, LV ejection fraction, and cardiac output were detected in rats of group 1 over three month of empagliflozin treatment; these changes were not observed in rats of the reference group (group 2).

Conclusion. Empagliflozin improves LV functional parameters and exercise tolerance in normoglycemic rats with experimental CHF. The impact of empagliflozin on LV remodeling needs further investigations.

EPICARDIAL ADIPOSE TISSUE THICKNESS AS A PREDICTIVE MARKER OF CORONARY ARTERY DISEASE

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Background: It has been demonstrated that an increased epicardial adipose tissue thickness is associated with visceral fat mass as a one of reasons the development of clinical cardiovascular disease.

Purpose: to estimate relation between thickness of epicardial adipose tissue (EAT) and risk factors of coronary artery disease (CAD) in North-West Region Russian population.

Methods: 120 community residents were enrolled: 64 males (53,3 %) and 56 females (46,7 %), age 58,7±1,1 years: 100 patients with CAD and 20 healthy subjects. CAD was diagnosed according to ESC guideline (2013). Waist circumference (WC), BMI, office blood pressure (BP), medical history was analyzed. Fasting glucose and lipid profile were measured. EAT was analyzed by standards echocardiogram. Statistical analyses were performed with SPSS 20.0 for Windows.

Results: Abdominal obesity (AO) was determined in 60% of responders, 79% were hypertensive, diabetes mellitus type 2 was observed in 20%, 41% had myocardial infarction and revascularization was performed for 41% CAD patients. EAT was significantly thicker in subjects with CAD, compared to healthy ones (9,6±0,03 mm vs 1,5±0,01 mm; p=0,001); in CAD fimales than in similar males (11,1±0,04 mm vs 8,4±0,02 mm; p=0,05); in hypertensive patients (10,3±0,04 mm vs 8,2±0,02 mm; p=0,05), in diabetic patients (13,8±0,03 mm vs 9,7±0,01 mm; p=0,05) and in patient with abdominal obesity (14,1±0,05 mm vs 7,9±0,02 mm; p=0,05). We revealed significant positive correlations between EAT thickness and age, WC, BMI, serum triglycerides level and cholesterol of VLDL (r=0,440; 0,248; 0,284; 0,390 and 0,280 accordingly; p=0,05).

Conclusion: Significance thicker of epicardial adipose tissue is associated with such risk factors of CAD as arterial hypertension, abdominal obesity, dyslipidemia, diabetes mellitus type 2 in North-West Region Russian population.

EPICARDIAL FAT, MARKERS OF INFLAMMATION AND FIBROSIS IN PATIENTS WITH METABOLIC SYNDROME

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Introduction. Visceral adipose tissue has proinflammatory and profibrogenic effects on cardiovascular system. Epicardial fat is localized near cardiomyocytes and may influence upon remodeling of the heart.

Aim. Study objective – to evaluate the epicardial fat thickness (EFT) and to reveal the possible relationship of this parameter with high sensitive C-reactive protein (hsCRP) and galectin 3 (Gal 3) as markers of inflammation and fibrosis in patients with metabolic syndrome (MetS).

Material and methods. 60 patients 35-65 years old with MetS according to the criteria IDF were examined. The control group was 60 persons without metabolic disorders and cardiovascular disease. Groups did not differ significantly by gender, age, eGFR (p>0,05). The examination includes: medical history, anthropometry, echocardiography, lipids, glucose, blood pressure, serum hs-CRP level (Immunoturbidimetric method) and Gal 3 (Enzyme immunoassay). The patients with acute and chronic inflammation, as well as with hs-CRP levels greater than 10 mg/L were excluded. The EFT was measured with transthoracic echocardiography over the free wall of the right ventricle, in at least two positions of the longitudinal and transverse parasternal.

Results. The epicardial fat thickness was more than 2 fold greater in the MetS compared with the control group (4,7±1,3 and 2,4±0,9 mm; p<0,001). Hs-CRP was more than 3 fold higher in the MetS compared with the control group (2,4±0,2 and 0,8±0,1 mg/L; p<0,001) and median of Gal 3 also was more higher in patients with MetS (0,48 [0,42;1,39] and 0,27 [0,24;0,32] ng/ml; p<0,001). Correlation analysis among all examined persons showed a strong positive correlation between EFT and diameter, volume of the left atrium and left ventricle mass index (r=0,64, 0,61, 0,51; p<0,001). Correlation between EFT, hs-CRP and Gal 3 was also strong positive (r=0,71, 0,61; p<0,001).

Conclusions. Epicardial fat in patients with MetS is thicker than in healthy people. Greater thickness of epicardial fat is associated with higher levels of markers of inflammation and fibrosis: high sensitive C-reactive protein and Galectin 3. Epicardial fat can influence on remodeling of the heart.

EXPERIMENTAL HYPERLIPIDEMIA IN RATS, OBTAINED DURING THE SELECTION OF RATS, WHICH IS DIFFICULT TO DEVELOP A CONDITIONED DRINKING REFLEX

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There is no doubt that for the initial screening of lipid-lowering drugs, models in experimental animals are required. However, outbred white rats are steady to the development of significant hyperlipidemia. In this regard, we have attempted to create a short model using the physiological characteristics of these animals. The study was performed in male rats, which were previously tested for the development of a conditioned drinking reflex.

Results. The use of a diet enriched with cholesterol causes individual differences in the accumulation of cholesterol in blood serum in the mongrel rats and its distribution in the lipoproteins, which may be due to the genetically determined characteristics of the animals. Hypersensitivity of the rat to a rich cholesterol diet is inversely related to the ability of the rat to develop a conditioned drinking reflex. It was shown that in rats with experimental hyperlipidemia it was difficult to produce a conditioned reflex in comparison with control animals. Easily trained animals from poorly trained differ in the content of cholesterol, both in serum of blood and in the synaptic membranes of brain neurons.

The determination of lipids in blood serum and in the liver showed that the initial serum cholesterol content was studied in rats that differed from those in untreated animals and were 45.8 and 63.2 mg/dl, respectively. The use of hypercholesterolemic diet showed that the trained animals were less sensitive to the effect of serum cholesterol concentration in comparison with untrained animals. With a 20-day hypercholesterolemic diet, rats with the high serum cholesterol content were 51.1 mg/dl, and in untreated – 84.4 mg/dl. There were differences in the liver also.

Conclusion. The preliminary selection as of the condition of elaboration of the conditioned reflex (trained and untrained) makes it possible to obtain stable moderate hypercholesterolemia in untrained animals after 10 days.

FACTORS OF CARDIOMETABOLIC RISK AND POLYMORPHIC VARIANTS OF THE MODIFIER GENES MADD AND GLA IN HYPERTROPHIC CARDIOMYOPATHY

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Background. Phenotypic manifestations of the hypertrophic cardiomyopathy (HCM) depends on genetic mutations, including co-existing genetic variants such as SNPs of modifier genes, and factors of cardiometabolic risk, in particular obesity.

Purpose. To study the influence of cardiometabolic risk factors and nonsarcomeric polymorphic variants on myocardial remodeling in patients with HCM.

Methods. The study group included 154 patients with HCM at the age 45 to 91 years (57.69 ± 11.19 years, men – 52%, women – 48%). A standard clinical – laboratory and instrumental methods of diagnostics were applied. Genotyping for SNPs rs2290149 and rs10838692 of the MADD gene was performed using real time PCR. The activity of the α-D-galactosidase enzyme in dried blood spots was determined by tandem mass spectrometry

(ESI-MS/MS). Also the 1 -7 exons and adjacent intron regions of the GLA gene were investigated. The control group included 288 healthy donors without cardiovascular diseases and other severe pathologies, matched by age and sex with the studied group.

Results. We observed a significant increase in frequency of TT genotype of rs2290149 and rs10838692 of the MADD gene in patients with HCM compared to healthy group (82.5% vs. 71.5%, p = 0.025 and 55.2% vs. 43.1%, p = 0.019, respectively). The allele frequency also differs for rs2290149 (T:C = 89.9%:10.1% in HCM and 82.3%:17.7% in control group, OR=0.520, 95% CI 0.339 to 0.798, p = 0.002) and for rs10838692 (T:C=72.4% : 27.6% in HCM and 62.2%: 37.8% in control, OR=0.626, 95% CI 0.463 to 0.846, p = 0.002). In 23 patients in which HCM combined with lesions of other organ systems, particularly with renal (microalbuminuria, proteinuria, decreased glomerular filtration rate), peripheral (acroparesthesia, pain in the limbs) and central nervous system (stroke at a young age), the skin (angiokeratoma), having an X-chromosome-linked disease, was carried out the screening for Fabry disease. The data obtained didn't show the reduce enzyme activity, mutations leading to disease is not established. In 5 patients was found polymorphisms in the intron and promoter regions of the GLA gene: rs3027584, rs2071397, rs2071228, rs2071225, rs3027585, rs3027589. Pre-obesity and obesity in patients with HCM were associated with increased LV posterior wall thickness (14,82 ± 3,6 mm versus 12,77 ± 3,69 mm, respectively, p <0,01), but not the LV mass index and the interventricular septum. Obese HCM patients had greater detection rate of the symmetrical left ventricular hypertrophy (64% versus 10 % in non-obese HCM patients, p<0,001).

Conclusions. The T allele and TT genotype of SNPs rs10838692 and rs2290149 of the MADD gene were associated with the presence of HCM in patients, but do not affect on the degree of myocardial hypertrophy. Pre-obesity and obesity in patients with HCM led to the significantly greater left ventricular posterior wall thickness, but not the septal wall. Symmetrical variant of myocardial remodelling was observed more often in obese HCM patients. The SNPs in the GLA gene in patients with HCM contributes to the formation of extracardiac manifestations typical for Fabry disease.

FATTY LIVER DISEASE BY ULTRASOUND IN POPULATION: PREVALENCE AND GENDER SPECIFIC DETERMINANTS

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Non-alcoholic (NAFLD) and alcoholic fatty liver disease (AFLD) have common components of pathogenesis and might be considered as indicator of cardiovascular risk. There are little knowledge about prevalence and mechanisms of FLD in Russia which is characterized by high CVD mortality and diverse patterns of alcohol intake. **Purpose:** We investigated prevalence of FLD by ultrasound and analyzed risk factors of steatosis in men and women in a population (Novosibirsk, Russia). **Methods:** In epidemiological survey, a random population sample of 2025 persons (870 women) aged 25-64 years was studied by ultrasound. The association of FLD with potential determinants was estimated in logistic regression.

Results: The prevalence of FLD was 20% in men and 19% in women. In men, its multivariable-adjusted predictors included: age, body mass index (BMI), triglycerides level (TG) as well as high occasional dose (≥120g of ethanol) – [OR(95%CI)] 2.6 (1.41-4.67), p=0.002 or frequent drinking more than once a week – 9.2 (4.55-18.46), p<0.001 (against non-drinkers. In women, in age-adjusted model FLD was associated with BMI, level of total and HDL-cholesterol, TG and diabetes mellitus. In multivariable-adjusted model the only association between FLD and BMI remained significant: 1.20 (1.14-1.25), p<0.001, for BMI ≥35 vs. <25) and had no association with any alcohol measures.

Conclusion: The prevalence of sonographic FLD in our sample was equal in men and women –20%, and comparable with data from other populations. The structure of FLD in our population was gender specific: NAFLD was predominant in women (2/3 of cases), but in men, AFLD and NAFLD were equal (6.2 %). In women, FLD was largely explained by BMI among other metabolic factors. In men, FLD was strongly predicted by frequency of alcohol intake and high dose/per session, and, to lesser degree, by age and metabolic indicators.

FEATURES OF CARDIAC REMODELING WITH ARTERIAL HYPERTENSION ASSOCIATED WITH TYPE 2 DIABETES MELLITUS

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The pathology of the cardiovascular system is noted in more than half of patients with diabetes mellitus (DM), while at the same time suggesting that changes in the cardiovascular system caused by diabetes are observed in 90-100% of patients. Myocardial damage in diabetes is a result of a combination of atherosclerotic processes In the coronary arteries, the presence of microangiopathies and neuropathies inherent in diabetes. However, clinical studies have shown that severe HF can occur in patients with diabetes even in the absence of signs of coronary atherosclerosis. The goal is to reveal the frequency of the spread of various variants of heart failure in type 2 diabetes mellitus combined with arterial hypertension

Material and methods. A closed cohort controlled study of 120 patients with arterial hypertension (AH) of stage I-II in combination with type 2 diabetes mellitus aged 50-59 years, of which 50 men (40%) and 70 women (60%) who agreed to Inclusion in the study. As a comparison group, 50 patients with isolated stage I-II AH were examined. The control group consisted of 50 healthy patients, comparable in gender and age. Echocardiography was performed on a Logic -5 XP ultrasound scanner with a 3.5-MHz sensor in the patient's position on the left side at an angle of 45 ° using standard techniques to determine the presence of left ventricular hypertrophy and the type of remodeling. The following models of the geometry of the left ventricle were distinguished: with normal geometry, concentric remodeling, concentric and eccentric types of left ventricular hypertrophy (LVH) .

Results. In patients with isolated hypertension, when compared with the control group, the following changes were observed: the thickness of the left ventricle walls increased with the unchanged size of its cavity, the mass of the left ventricle myocardium increased (including its indexed index), the volume of the left atrium and its index. The type of the geometric model, therefore, corresponds to the concentric (increase in the thickness of the walls with an unchanged cavity) with an increase in the relative thickness of the walls of the left ventricle. The association with diabetes changes the type of heart reaction. With a comparable thickness of the walls of the myocardium, the left atrium and left ventricular mass continue to increase, the dilatation of the left ventricular cavity appears, the ejection fraction appears, which corresponds to an eccentric geometric model with a decrease in the relative thickness of the myocardial wall to normal (more precisely, «pseudonormal») digits and a decrease in systolic function . In the study group, hypertrophy of the left ventricle was 55%, and the main type of LVH was concentric. The presence of diabetes mellitus increases the incidence of LVH to 66% with an increase in the percentage of eccentric LVH threefold, from 15% to 44%. Moreover, this type of geometry in patients with diabetes mellitus is accompanied by a progression of the left atrial enlargement ($p < 0.05$) and a decrease in the ejection fraction ($p < 0.05$), which makes it possible to evaluate this transformation as peremptorily nonadaptive.

Conclusions. The association of arterial hypertension with diabetes changes the type of heart reaction. The presence of diabetes mellitus increases the incidence of LVH to 66% with an increase in the percentage of eccentric LVH threefold, from 15% to 44%. This type of geometry in patients with diabetes mellitus is accompanied by a progression of the left atrial enlargement and a decrease in the ejection fraction, which makes it possible to evaluate this transformation as an early stage in the development of heart failure.

FIRST GRADE ARTERIAL HYPERTENSION AND OBESITY

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Objective. To specify hemodynamic and metabolic disorders in patients with first grade arterial hypertension and obesity; to assess their prognostic value.

Design and methods. 74 patients with first grade arterial hypertension (44 with accompany obesity) and 56 persons with optimal or normal blood pressure without obesity were included in this study. At baseline and 71,3±10,5 months later body mass and office blood pressure were measured, daily blood pressure monitoring was done. Additionally at baseline color doppler sonography of the carotid and vertebral arteries and oral glucose tolerance test were performed; plasma insulin, insulin-like growth factor, vascular endothelial growth factor and erythropoietin concentrations were measured.

Results. Obesity in patients with first grade arterial hypertension is characterized by lowering of peak systolic blood flow velocity in vertebral arteries in female, augmentation of daily blood pressure variability, reduced daily indexes of systolic and diastolic blood pressure, hyperinsulinemia/insulin resistance, decreased plasma insulin-like growth factor concentration, increased concentration of vascular endothelial growth factor and erythropoietin in plasma. Baseline hyperinsulinemia leads to worsening of medium-term prognosis in hypertensive patients. Baseline body mass index didn't affect prognosis. Present direct correlation between initial level of vascular endothelial growth factor and reduction in body mass index in follow up. Patients with higher concentration of vascular endothelial growth factor were attached to regular physical exercise.

Conclusion. Accompany obesity leads to augmentation of hemodynamic and metabolic disorders in patients with first grade arterial hypertension which have negative effects to medium-term prognosis in these patients. Simultaneously obesity may initiate protective mechanisms in hypertensive patients.

GLUCOSE-LOWERING THERAPY IN PATIENTS HOSPITALIZED WITH CONGESTIVE HEART FAILURE IN ROUTINE CLINICAL PRACTICE

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Background: This study was aimed to investigate glucose-lowering therapy (GLT) in patients with known diabetes mellitus (DM) hospitalized with congestive chronic heart failure (HF) of different etiology.

Methods: We used administrative data to retrospectively identify patients of cardiology departments of the First clinical hospital of Arkhangelsk with DM and decompensated HF. 136 patients were included in the final analysis. The majority was female (61%).

Results: The median (25^{th}, 75^{th} percentile) age of 136 study patients was 74.5 years (64.25; 81.00). A large proportion of patients (28.7%) didn't receive GLT before hospitalization, 50% were treated with oral therapy, while 14% received insulin alone and 7.4% received insulin in combination with oral therapy. In 89% of patients, therapeutic strategies had not been changed during whole period of hospitalization. Admission glucose was significantly higher in patients received insulin therapy (11.74 (8.70; 17.97) than patients without GLT (6.19 (5.01; 8.18) (p=0.0089).

In 4.4% oral drugs were changed to insulin and the same per cent of patients were underwent correction of insulin therapy, 1.5% of patients without GLT were prescribed insulin therapy and in 0.7% oral drugs were stopped. Changing of GLT was significantly associated with admission glucose (rs=0.184, p=0.063) and glycemic variability: SD (rs=0.287; p=0.002), CV (rs=0.246; 0.007), mean glucose level (rs=0.227; p=0.013). But changes in GLT

weren't based on clinical profiles: peripheral edema (rs=0.25; p=0.77), pulmonary edema (rs=0.129; p=0.133), hydrothorax (rs=0.154; 0.123). Furthermore, we didn't find the association between changing of GLT and renal function: creatinine level (rs=0.64; p=0.483) and eGFR using CKD-EPI (rs=-0.70; p=0.421).

Conclusion: The results of this study demonstrate strategy of GLT in patients with congestive HF and DM in routine clinical practice. Effects of this therapy on the risk of cardiovascular mortality and DM complications require further study.

GLUCOSE TOXICITY AND PERIPHERAL INSULIN RESISTANCE IN PATIENTS WITH TYPE 2 DIABETES: THE WAY TO OVERCOME

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Background and aims: β-cell glucose toxicity and peripheral insulin resistance are serious obstacles to antidiabetic therapy in patients with diabetes mellitus type 2 (DM2). Hypoglycemic effect of SGLT-2 inhibitors is mediated by lowering of glucose reabsorption in kidney and does not depend on β-cell function and peripheral insulin sensitivity. The aim was to study parameters of β-cell secretory activity and peripheral insulin resistance in DM2 patients received dapagliflozin.

Materials and methods: 27 patients with uncontrolled DM2 were included in our study. Weight, height, body mass index (BMI), blood pressure (BP) were assessed. Fasting plasma glucose (FPG) was measured by glucose oxidase method. HbA1c was measured by immunochemistry analysis. Insulin was measured by RIA. Parameters listed above were assessed at baseline and after follow-up period. HOMA-B was calculated as 20 × fasting insulin {μIU/ml}/FPG {mmol/l} − 3.5 in group of patients without insulin therapy (n=14). Insulin resistance was estimated by the HOMA index (HOMA-IR), where HOMA=fasting insulin×FPG/22.5 in all patients. Data were analysed using STATISTICA. Data were expressed as mean±standard deviation. ANOVA repeated method was used.

Results: There were 33.3% men and 66.6% women. The average age was 55.14±2.52 year old. Average weight was 99.12±3.94 kg. The average BMI was 35.11±1.19. All patients have had obesity or overweight. DM2 duration was 11.1±1.2 years. FPG was 12.4±0.5 mmol/l. HbA1c was 10.3±0.3%. No patients have had target HbA1c levels. At baseline HOMA-B was 40.80±10.12 and HOMA-IR was 12.27±1.24. All patients received dapagliflozin 10 mg once daily. There was improved glycemic control with dapagliflozin therapy. FPG and HbA1c levels were decreased to 7.74±0.31 mmol/l and 8.9±0.2, respectively. Weight was decreased by 6.02±9.91 kg. Systolic and diastolic BP levels were decreased by 12.6 mmHg (p=0.0002) and 5 mmHg (p=0.017), respectively. HOMA-B was increased to 59.7±13.4 (p=0.007). HOMA-IR was decreased to 5.42±0.79 (p=0.0004).

Conclusion: Dapagliflozin treatment led to improved glycemic control, improving of β-cell secretory activity and reducing of peripheral insulin resistance in patients with DM2.

IMPACT OF METABOLIC DISORDERS ON THE DEVELOPMENT OF INFECTIOUS COMPLICATIONS IN ANGIOSURGERICAL PATIENTS

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Relevance: The development of surgical site infection (SSI) is a dangerous complication in the postoperative period, which not only leads to an increase in hospitalization, but it is usually accompanied by high amputations, and may even result in death.

The aim of this study was to identify the risk factors for the development of SSI in the postoperative period in patients with peripheral atherosclerosis.

Materials and Methods: The research is based on the observation of 57 patients with PAD who underwent reconstructive surgery on the main vessels. Patients were divided into the main and control groups, depending on the presence or absence of infectious complications after the surgical intervention. In 34 patients (main group) aged from 52 to 80 years (mean age 66.2 ± 9 years), SSI signs were noted, 23 patients (control group) aged from 47 to 81 years (mean age 60.2 ± 10,4 years), no SSI complications were noted. Statistical processing was performed using «STATISTICA-10» software package. The value «p <0.05» is indicated as statistically significant.

Results: The presence of diabetes (type 2, decompensated) significantly increases the risk of SSI development (p <0.01). In the main group, the average blood glucose level was 6.23 mmol / L, in the control group – 5.79 mmol / L (p <0.05). Also in the main group, the more pronounced glucose variability was noted, compared with the control (p <0.05). Stage 3 hypertensive disease in the main group was more common than in the control group (p <0.01). The target value of systolic blood pressure in the main group was 158.5 ± 15.5 mm. In the control – 138 ± 15.5 mm. (P <0.01). The increase of atherogenic factor was more often noted in the main group compared with the control group (3.5 ± 0.9 v / s 2.7 ± 0.7, p <0.01). Visceral obesity was more frequently registered in patients of the main group (p <0.01). The presence of critical ischemia was significantly more frequent among patients in the main group (p <0.01). Visceral obesity was noted in the main group much more frequently than in the control. Metabolic syndrome was recorded in 25 patients in the main group, 5 in the control group (p <0.05).

Conclusions: The presence of metabolic syndrome and its components affects the development of infectious complications in patients with the peripheral arterial disease. Correct perioperative patients' management and pharmacological correction of risk factors help to reduce the development of adverse events in the early postoperative period.

INTERRELATION BETWEEN GLP-1 LEVEL AND GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background and aim: Type 2 diabetes mellitus (DM) is one of the leading problems of contemporary medicine. Certain aspects of pathogenesis of this disease still remain topics of debates. Thus it is well-known that incretin effect is impaired in type 2 DM. But whether it is a consequence of glucagon-like peptide-1 (GLP-1) altered secretion by gut L-cells or it's defective interaction with specific GLP-1 receptor on pancreatic beta-cells still remains contradictory. Besides there is very poor information about dynamics of GLP-1 level during treatment of DM, in conditions of different glycemic control and use of different groups.

Aim of our study was to evaluate GLP-1 level in patients with type 2 DM with poor glycemic control and to investigate it's dynamics during different DM pharmacotherapy.

Materials and methods: Patients with type 2 DM aged 40-75 (n=30) with unsatisfactory glucose control on metformin monotherapy were included in the study. They had been receiving effective hypotensive and hypolipidemic therapy at least 3 months before the beginning of the study. Then metformin dose was titrated for 3 months, afterwards patients were divided into group 1 (n=15) (those who reached target HbA_{1c} and continued metformin monotherapy for 6 months more), and group 2 (n=15) (those who did not reach target HbA_{1c} and were administered liraglutide in addition to metformin, for 6 months more). GLP-1 level was assessed at baseline and every 3 months.

Results: The baseline level of GLP-1 was reduced in all patients and didn't differ significantly in groups 1 (4.56 (3.95, 6.66) ng/ml) and 2 (4.96 (4.21, 7.7) ng / ml). GLP-1 was increased in group 1 in 3 month (7.6 (5.15, 12.9) ng / ml), comparing with baseline level, p<0,05. The level of GLP-1 didn't change in group 2 in 3 months of metformin monotherapy under still poor glycemic control (3.84 (3.55, 4.61) ng / ml), p> 0.05. Liraglutide administration led to significant increase of GLP-1 in group 2 (18.39 (7.48, 16.55) ng / ml) in 6 months. No further dynamic of GLP-1 level was observed in group 1 in 6 months (6,03 (4,92;8,52) ng/ml). Importantly, GLP-1 level did not differ in groups 1 and 2 in 6 months when all patients reached euglycemia.

Conclusions: Glycemic control improvement is associated with increase of GLP-1 level. A choice of drug for DM treatment does not influence GLP-1 level dynamics itself. Type 2 DM is probably associated with reversible L-cells dysfunction connected with hyperglycemic condition.

IVABRADINE AND OUTCOMES IN PATIENTS WITH ACUTE DECOMPENSATED SYSTOLIC HEART FAILURE

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Background. Elevated heart rate represents an important risk factor for adverse outcomes in patients with heart failure. As heart rate is associated with hospital admissions and mortality, the open question is whether early treatment to achieve heart rate reduction with an If-channel inhibitor – ivabradine could reduce the high readmission rate and mortality.

Objectives. We aimed to assess the effect of heart-rate reduction by the selective sinus-node inhibitor ivabradine on outcomes in heart failure.

Material and methods – A prospective observational study that included 50 consecutive patients with hospitalized systolic heart failure, sinus rhythm and heart rate >70 b/min in whom ivabradine was administered during hospitalization or early after discharge. Clinical data, echocardiography, follow-up events were recorded at baseline and after 6 months, 12 months of follow-up; 1 year mortalty and rehospitalization rates for heart failure were compared with ivabradine and placebo groups. Patients were randomly assigned by computer-generated allocation schedule to ivabradine titrated to a maximum of 7·5 mg twice daily or matching placebo.

Results. 50 patients were randomly assigned to treatment groups (26 ivabradine, 24 placebo). Ivabradine was administered in 52,1%. Median follow-up was 12 months. 11 (42%) patients in the ivabradine group and 16 (66%) of those taking placebo had a hospitalization in one year period. The hospitalization rate (number of hospitalization) in the placebo group was much higher than in the ivabradine group (9 [37,5%] vs 3 [11%]; p<0,001), and the deaths due to heart failure (14 [58%] *vs* 1 [3,8%]. One year all cause mortality was 30%. Fewer serious adverse events occurred in the ivabradine group (3 events) than in the placebo group (8 events, p<0,001).

Conclusions. Ivabradine therapy in patients hospitalized for decompensated heart failure improve of clinical outcomes,well tolerated, reduce mortality and rehospitalizations.

Keywords: heart failure, decompensation, heart rate, ivabradine, mortality, hospitalization

LIPOPROTEIN(A) IS ASSOCIATED WITH SEVERE PERIPHERAL ATHEROSCLEROSIS

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Aim. The objective of the study was to evaluate the association of lipoprotein(a) [Lp(a)] with peripheral and carotid atherosclerosis.

Methods. We examined 101 patients (mean age 62.5±9.6 years, 86 (85%) males) with severe peripheral atherosclerosis (atherosclerotic lesions with at least one stenosis of low limb arteries ≥50%) and 211 patients (mean age 66.1±10.2 years, 146 (69%) males) with severe (at least one stenosis of carotid arteries ≥50%) carotid atherosclerosis. The level of Lp(a) was measured by enzyme-linked immunosorbent assay.

Results. The level of Lp(a) and prevalence of high Lp(a) level were significantly higher in patients with peripheral atherosclerosis compared to patients with carotid atherosclerosis, respectively: 52±49 mg/dl and 40±44

mg/dl, p=0.03; 60 (59%) and 94 (45%), p=0.02. The odds of severe peripheral atherosclerosis in the presence of high Lp(a) level was 1.8 (95% confidence interval, 1.1-2.9, p=0.01). The frequency of smoking in patients with peripheral atherosclerosis was higher than in patients with carotid atherosclerosis: 69% (70 patients of 101) versus 39% (83 patients of 211), p<0.01. According to the data of multiple regression analysis only Lp(a) and smoking were independent predictors of severe peripheral atherosclerosis.

Conclusion. Elevated lipoprotein(a) level is associated with severe peripheral atherosclerosis rather than with severe carotid lesions.

LIRAGLUTIDE ATTENUATES NEUROGLIAL DAMAGE AND ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH METABOLIC SYNDROME

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Background and aim: Metabolic syndrome (MS) in one of the leading healthcare problems of nowadays. Chronic brain ischemia is much more frequent and severe in this cohort of patients than in the population. This requires a search for a drug that not only has an influence on MS components, but also demonstrates neuroprotective effect. Liraglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, decreases blood glucose level, lowers blood pressure and diminishes dyslipidemia, thus having influence on all MS components. Moreover GLP-1 receptor agonists have demonstrated cardioprotective effect. Specific receptors are widely presented in central nervous system and in endothelium, therefore these drugs might also have neuroprotective effect.

The aim of our study was to investigate potential neuroprotective effect of GLP-1 receptor agonist liraglutide in MS patients.

Materials and methods: Patients with MS aged 40-75 (n=53) with unsatisfactory glucose control on metformin monotherapy were included in the study. They had been receiving effective hypotensive and hypolipidemic therapy at least 3 months before the beginning of the study. Then metformin dose was titrated for 3 months, afterwards patients were divided into group 1 (n=34) (those who reached target HbA_{1c} and continued metformin monotherapy for 6 months more), and group 2 (n=19) (those who did not reach target HbA_{1c} and were administered liraglutide in addition to metformin, for 6 months more). At baseline and every 3 months following parameters were assessed: von Willebrand factor (vWF) activity, endothelin-1, tissue plasminogen activator (tPA), plasminogen activator inhibitor-1 (PAI-1) as endothelial dysfunction markers and neuronspecific enolase (NSE), S100 protein as neuroglial damage markers.

Results: Primarily all patients represented a total group. But we discovered that patients who afterwards formed group 2 had significantly higher baseline levels of NSE (44.2 (28.3;46.7) μg/L), tPA (6.55(4.54;9.15) ng/ml), PAI-1 (122.8(88.18;129.3) ng/ml) and endothelin-1 (3.01(1.97;3.15) pmol/L), comparing with the future group 1 (NSE 24.66 (21.7;36.4) μg/L, tPA 5.12(4.7;6.1) ng/ml, PAI-1 96.2 (31.6;105.0) ng/ml and endothelin-1 0.88 (0.86;1.27) pmol/L). Glycemic control improvement resulted in decrease of the factors in 3 months in both groups. Liraglutide administration led to additional reduction of the factors in group 2, comparing to group 1, with similar glucose level. Total lowering of NSE during 9 months of study was 36.33(27.65;38.76) and 16.33(11.59;23.7) μg/L in groups 2 and 1, respectively, tPA 3.35(3.03;4.0) and 0.85(0.56;1.42) ng/mL, PAI-1 77.16(66.35;109.2) and 46.45(10.2;70.1) ng/mL, endothelin-1 2.92(1.858;3.087) and 0.58(1.14;0.754) pmol/L, p<0.05.

Baseline level of vWF activity did not differ significantly in groups 2 (116.1(91.8;201.4)%) and 1 (132.1(89.6;144.8)%), p>0.05. It decreased significantly only in group 1 in 3 months. Administration of liraglutide resulted in significant lowering of vWF activity and total reduction for 9 months was 50.8(27.55;77.2;) and 30.7(25.6;38.1)% in groups 2 and 1.

No difference was found in S100 baseline level in groups 2 and 1. It decreased in both groups in 3 months, but liraglutide did not cause beneficial reduction for 9 months ((85.38(74.75;181.5) ng/l in group 2 and 124.05(104.65;169.15) ng/l in group 1, p>0.05).

Conclusion: Glycemic control improvement ameliorates endothelial dysfunction and neuroglial damage. Nevertheless liraglutide has an independent neuroprotective effect, not related to glucose-lowering action. High level of NSE, tPA, PAI-1 and endothelin-1 might serve an indicator of endothelial and neuroglial damage in MS and require intensification of therapy, including that, having neuro- and endothelioprotective properties.

METABOLIC SYNDROME AND SLEEP APNEA

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Background: It has been suggested that obstructive sleep apnea syndrome (OSAS) independently influences glucose metabolism. Nevertheless studies with OSAS patients which have investigated the impact of continuous positive airway pressure (CPAP) therapy regarding insulin-sensitivity and glucose metabolism have shown heterogeneous results.

Objectives: the aim of the study was to assess the effects of treatment with (CPAP) in patients with Metabolic Syndrome (MS) accompanied with OSAS. We studied 43 patients, aged 41 to 65 with type 2 diabetes, obesity, mean body mass index (BMI) 27.2 kg/m², hypertension, severe OSAS, mean apnea hypopnea index (AHI) 45,21± 3,28 events per hour. All patients received CPAP-therapy. The effect of CPAP was followed-up after 6 months – treatment. Various endpoints were investigated. The response was assessed from changes between baseline and follow-up measures of BMI, HbA1c value, doses of hypoglycemic drugs, level of blood pressure, functional status/general health.

Results: finally after 6 months CPAP treatment we observed the improvement of functional status/general health of all 43 (100%) subjects, in 38 subjects (88%) – the reducing of hypertension, in 15 (35%) – reducing in HbA1c and doses of hypoglycemic drugs ($p < 0.05$), at the same time we did not reveal any changes in BMI ($p>0.05$).

Conclusion: the effects of CPAP support the hypothesis that OSAS influences glucose metabolism. Further long-term randomized controlled trials defining changes of insulin resistance are needed.

MONITORING THE STATUS OF THE COGNITIVE FUNCTIONS AND RISK FACTOR PREVALENCE OF CARDIOVASCULAR DISEASES IN PATIENTS WITH CAROTID ATHEROSCLEROSIS

Duma S

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Cognitive disorders (CD) are an essential satellite of the most cardiovascular disease (CVD). According to the severity of the CD: mild cognitive impaitment (MCI) and dementia (D) . Traditionally, risk factors (RF) CD include age, family history of CD, bad habits, CVD, metabolic disorders.

Objective: evaluation of mechanisms relations RF CD of CVD. Research objectives: 1. Evaluation of prevalence and severity of the CD and the RF CVD in a population of patients with clinically confirmed carotid atherosclerosis (CA) aged 55-78 years .2. Assessing the role of social and other RF CVD in the formation of CD.

M**aterials and Methods:** 500 subject were evaluated for the open-label study with disorders of lipid metabolism and confirmed CA (the presence average of atherosclerotic plaques up to 35% of the total clearance of the carotid artery during ultrasound assessment). Following RF were assessed: systolic (SBP) and diastolic (DBP) blood pressure, pulse heart per minute (P), Quetelet index, physical activity in minutes per week (PA), consumption of alcohol per milliliter per week). The average age was 62.2 years. Additionally cognitive function was assessed for all enrolled subjects using neuropsychological tests confirming the degree the CD: «5 words» with the assessment of the immediate and delayed recall (the rate of not less than 8 words in total); mokotest (26 points or

less); test «clock» -below 10 points. According to test results the patients were divided into subgroups according to the severity of the CD: MCI, D. The prevalence of CVD risk factors was evaluated in the general group (with CA) and an additional group (CA and CD).

Results: In general group of patients with CA averages were- 129.3 mm Hg SBP, DBP- 81.38 mmHg, P. 71.56. PA was 454.26 minutes (m. 455.3; f.454.1); Quetelet index – 29.6 (m. 27.4; f. 29.9) with no statistically significant difference. Among other RF more frequent consumption of alcohol a week for men was revealed (m. 88,5ml; f. 36.2 ml) (p <0,001). 110 patients (32%) detected by neuropsychological testing CD. The average values during the test «5 words» -6.69; Mokatest- 23.9 , test «hours» – 7.8 . Men: MCI 95.2%; D – 4.8%. Women: MCI-93.5%; D- 6.5%. Separately the prevalence of CVD RF has been studied in patients with CD. Arterial hypertension (AH) is the most frequent RF in patients with CD. AH was revealed in 114 subjects, 71% compared to the overall group with only CA 52% (p <0,001). In subgroups with MCI 33.9%; D -6.1% prevailed the higher levels SBP (p <0,001), compared with DBP. Diabetes mellitus revealed in the group of women with MCI 13.1% (p <0,05).

Conclusions: 1. The incidence of CD in patients with CA 32%, prevailed the MCI (m.95.2%, f.93.5%). 2. The most significant RF in the group with CD were SBP (p <0,001); diabetes in the subgroup of women with MCI (p <0,05), the consumption of alcohol a week for men (p <0,001).

NAFLD AND INTRAABDOMINAL FAT THICKNESS IN PATIENTS WITH METABOLIC SYNDROME

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Objective: to study the diagnostic value of intraabdominal fat thickness (IFT) in the diagnosis of NAFLD in metabolic syndrome (MS).

Materials and methods. 803 patients with MS were investigated in age 60,28 (53;67) years, 299 men and 504 women. Anthropometric, biochemical and ultrasound investigations were provided. MS was diagnosed in the presence of central obesity (waist circumference (WC) >80 cm in women and >94 cm in men) and two additional criteria from: arterial hypertension, triglycerides (TG) more than 1,7 mmol/l, LDL greater than 3,0 mmol/l, HDL in women <1,2 mmol/l, in men <1,0 mmol/l, fasting plasma glucose level more than 6,1 mmol/l or impaired glucose tolerance. Exclusion criteria were viral and alcoholic etiology of liver damage. The IFT was measured during ultrasound investigation of abdomen. The control group included 70 patients without MS (40 men and 30 women). Statistical analysis was performed using the software package Statistica 10.0.

Results. WC was 107,2 (100;113) cm in men, 107,7 (100; 114) sm in women. Arterial hypertension was present in all patients. Disorders of carbohydrate metabolism were diagnosed in 433 patients (54%): diabetes mellitus type 2 – in 290 people, impaired glucose tolerance – in 69, impaired fasting glucose – in 74 patients. The level of triglycerides was 2,03 (1,29;2,38) mmol/l, LDL – 3,7 (2,9; 4,4) mmol/l, HDL 1,07 (0,89;1,22) mmol/l and 1,28 (1,02;1,49) mmol/l in men and women respectively. The IFT was significantly higher in men: 58,5 (47,4; 67) mm versus 50,9 (39;60) mm in women (p=0,000008).

NAFLD was detected equally often in men (44,7%) and women (45,2%) with MS. Gender differences in the prevalence of liver steatosis and NASH was not identified. In patients without MS NAFLD was less frequent (12,5% among men and 10% among women). The control group significantly differed from the group of MS, not only in the size of liver right lobe (p=0,0001 for men and p=0,00002 for women), but also in the size of the pancreatic head (p=0,000003 for men and p=0,000001 for women), indicating the formation of steatosis of the pancreas in MS. NAFLD was found in significantly younger age in men and women. The main component of MS (WC) was significantly higher in NAFLD in both sexes. The IFT in men with MS without NAFLD was significantly less than in men with hepatic steatosis (52(42;63) mm vs 64(52;70) mm, p=0,0007), and than in NASH (52(42;63) vs 66,5 mm(58,5;76) mm, p=0,01). In women with MS without NAFLD the IFT was also significantly lower than in patients with liver steatosis (44(36,5;54,5) mm vs 54(42;64) mm, p=0,002).

The ROC analysis, performed to establish the prognostic significance of the IAF in the diagnosis of NAFLD, showed the following results. In men, the sensitivity of the IFT in the diagnosis of NAFLD was 80% (specificity 31,6%), the AUC was 0,81; which reflects the very good quality predictive models. At the same time, the sensitivity of BMI in the diagnosis of NAFLD was 47,6%, WC- just 10,5%. In women the IFT predicts NAFLD with a sensitivity of 100% (specificity of 88,8%), the AUC was 0,88; the same as in men reflects the very good quality predictive models. WC shows sensitivity of 31,4% in the diagnosis of NAFLD.

Conclusion. Thus, the measurement of IFT is sensitive in the diagnosis of NAFLD, it is acceptable for use in screening for liver disease and exceeds the diagnostic value WC and BMI, which confirms the role of visceral fat depots but not general adiposity in the development of comorbidity in MS.

NERVE GROWTH FACTOR IN PATIENTS WITH ARTERIAL HYPERTENSION: THE ROLE OF OBESITY, ANXIETY AND PHYSICAL INACTIVITY

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Nerve growth factor (NGF) represents the family of neurotrophic factors. NGF participates in development and maintenance of neurons in peripheral and central nervous system, also regulates the activity of immune cells, fibroblasts, epithelial cells, pancreatic beta cells, adipose tissue cells and cardiomyocytes. NGF influences hypothalamic and brainstem noradrenergic nuclei, participating in the central regulation of autonomic nervous system and stress response. The role of NGF in pathogenesis of metabolic syndrome associated diseases such as atherosclerosis, arterial hypertension (AH), diabetes mellitus, heart failure, as well as the possibility of therapeutic use of neurotrophic factors in the treatment of these diseases is a subject of particular interest during the recent years.

Aim. To study NGF serum levels in patients with AH and obesity, depending on psycho-emotional status and physical activity.

Material and methods. 76 male patients with AH (mean age 46.75±0.56 years) were enrolled. Group 1 included 36 patients with AH and obesity (mean body mass index (BMI) 31.82±0.32 kg/m^2), group 2 – 40 AH patients without obesity (mean BMI 25.32±0.10 kg/m^2). Control group consisted of 26 persons without AH, obesity, cardiovascular and metabolic diseases (mean age 42.58±1.45 years, mean BMI 23.19±0.31 kg/m^2). Serum concentrations of NGF β-subunit were determined by enzyme linked immunosorbent assay. The level of reactive and personal anxiety was measured using a Spielberger-Khanin questionnaire. To assess physical activity a brief international questionnaire on physical activity (IPAQ) was used.

Results. In group 1 mean NGF serum level (0.94±0.28 pg/ml) was significantly increased compared to group 2 (0.21±0.06 pg/ml; p=0.018) and control group (0.16±0.06 pg/ml; p=0.02). The highest level of NGF was revealed in patients with AH and obesity lacking physical activity (1.26±0.44 pg/ml). This subgroup of patients also had considerably increased levels of reactive and personal anxiety compared to other subgroups. Correlation analysis showed inverse association between NGF serum concentration and the level of reactive anxiety ($r = -0.50$; $p = 0.03$) and personal anxiety ($r = -0.42$; $p = 0.08$).

Conclusion. The data obtained are suggestive for the involvement of NGF in neurohumoral regulation in AH associated with obesity, physical inactivity and increased anxiety as a stress-limiting mediator providing adaptation to chronic psycho-emotional stress. The increase of NGF serum concentrations in obese AH patients could be caused by direct neurotropic effects of adipokines. Therewith, determination of the exact role of NGF in complex pathophysiological interrelationships between AH, obesity, psycho-emotional status and physical activity requires further researches.

NEW LIPID-LOWERING AGENT K-312 INCREASES PHOSPHORYLATION OF AMP-ACTIVATED PROTEIN KINASE: A POTENTIAL MECHANISM FOR PCSK9 REDUCTION

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Background: K-312 is a cholesteryl ester transfer protein (CETP) inhibitor, being developed clinically in the United States for dyslipidemia. We previously reported that oral administration of K-312 in cholesterol-fed New Zealand White rabbits lowered LDL-C and increased HDL-C. Targeted proteomics analysis of plasma Proprotein convertase subtilisin/kexin 9 (PCSK9) demonstrated that K-312 decreased plasma PCSK9 concentrations in those rabbits, as a possible mechanism for LDL-C lowering. The present study has investigated the underlying mechanism by which K-312 decreases PCSK9.

Methods and Results: K-312 decreased PCSK9 expression by reducing its promoter activity in human hepatoma cell line HepG2. PCSK9 promoter harbors sterol regulatory element where active forms of sterol-regulatory element binding proteins (SREBPs) bind. K-312 treatment decreased active forms of SREBP-1 and SREBP-2 (western blotting) and binding of SREBP-1 and SREBP-2 to SRE of the PCSK9 promoter (chromatin immunoprecipitation), suggesting that the suppression of PCSK9 expression by K-312 involves SREBP-1 and SREBP-2. We also examined phosphorylation of AMPKα, which regulates gene expression and/or activities of proteins associate with lipid metabolism including SREBPs. K-312 treatment dose-dependently increased phosphorylation of AMPKα in HepG2 cells, which may contribute to lower PCSK9 levels by decreasing expression of SREBP-1 and SREBP-2.

Conclusion: The CETP inhibitor K-312 suppresses PCSK9 expression possibly via AMPKα phosphorylation. K-312 may serve as a novel therapy for dyslipidemia and cardiovascular disease.

OBSTRUCTIVE SLEEP APNEA LINKING SUDDEN CARDIAC DEATH IN MALE METABOLIC SYNDROME PATIENTS

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OBJECTIVES:

This study sought to identify the electrocardiographic markers of sudden cardiac death (SCD) associated with obstructive sleep apnea (OSA) in male metabolic syndrome (MS) patients.

BACKGROUND

Epidemiologic correlation between OSA and MS has been determined in multiple studies growth with OSA severity. Earlier the combination of OSA & MS has been referred to as «syndrome Z». However it is discussed if OSA might be an independent additional MS factor. Depending on the severity of OSA it raises the risk of SCD up to four times. Unfortunately, mechanisms of SCD in MS with OSA insufficiently studied.

MATERIALS AND METHODS

We included 112 male patients with MS, 85 of whom suffered OSA (apnea/hypopnea index (AHI) > 5 per hour). All OSA cases were divided in 3 groups – mild (N=28), moderate (N=28), severe (N=29) – depending on AHI severity. Controls were 31 male MS patients without OSA. We deployed late ventricular potentials: QRS duration (total QRS), low amplitude signal -duration of the terminal part of the QRS complex with an amplitude below 40

μV- (LAS-40), root mean square signal amplitude of the last 40 ms of the signal (RMS-40) via signal averaged electrocardiography as well as microvolt T-wave alternans (TWA) as tools of myocardial vulnerability identification .

RESULTS

By the duration of the total QRS complex, there were no significant differences, however, one can judge the tendency to increase the duration of the complexes in OSA cases. At the same time, there were significant differences in the LAS-40, RMS-40 and TWA in patients with respiratory disorders.

As a result of the correlation analysis, high-strength bonds were found between mean nocturnal saturation and the degree of TWA ($R = 0.72$, $p < 0.01$), nadir nocturnal saturation ($R = 0.75$, $p < 0.05$), nocturnal saturation variability ($R = 0.87$, $p < 0.05$), nocturnal desaturation burden ($R = 0.92$, $p < 0.01$) as well as the mean force relationship between the AHI and total QRS ($R = 0.51$, $p < 0.05$).

CONCLUSIONS

The revealed differences indicate the myocardium electrical heterogeneity and can be regarded as prognostically unfavorable indicators of sudden cardiac death in metabolic syndrome males with obstructive sleep apnea. AHI, as well as our findings- nocturnal saturation variability and desaturation burden – implicate undersaturated patients could be at higher risk of arrhythmic death. However nocturnal saturation variability and desaturation burden might be novel risk factors for SCD.

POSSIBILITIES OF USING THE METHOD OF MEASURING AUTOFLUORESCENCE WITH THE SPECTROMETER FOS 1 IN THE EARLY DIAGNOSIS OF MICROVASCULAR INJURY IN TYPE 1 DIABETES

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Background. A multipurpose fiber fluorescence–reflection spectrometer with multiwave excitation FOS-1 (prototype of the current AGE Reader, Diagnopticts BV, Netherlands) is intended for studies in autofluorescence (AF) of the skin, reflecting the content of andvanced glycation end products (AGEs) and the oxidation state. AGEs and oxidative stress are two main contributors of the development of diabetic complications. Intensive accumulation of AGEs in tissues occurs with various pathological conditions, which determines the complexity of using the method of their determination in the early diagnosis of diabetic microvascular complications. The variability of glycemia is powerful inducer of oxidative stress, at present the evaluation of its relationship with the AGEs is poorly understood and can be significant. At present, it is necessary to study the factors and conditions affecting the level of AGEs for creating a standardized evaluation system (for example, the age scale of norms), to study the role of AGEs in the early identification of various complications of diabetes. The aim was to determine the diagnostic significance of measuring AF of the skin with the spectrometer FOS-1, to evaluate the possibilities of using this method in patients with type 1 diabetes for early noninvasive diagnosis of microvascular complications.

Methods. Skin AF was assessed by the FOS-1. We noninvasively measured skin autofluorescence in 13 type 1 diabetic patients (age 29,2 [23;32] years, diabetes duration 11,9 [4;18] years) and 43 control subjects (age 30,6 [25;35] years), comparable by age, gender, BMI, the skin reflection coefficient (R). All studied individuals underwent routine laboratory tests, level of glucose in capillary blood was measured during the day at 9 points with further calculation of glycemic variability.

Results. Due to the lack of possibility to use the patented device with the aim of direct comparison of the results, comparison was made by re-measuring the AF in the healthy control group and with similar groups examined on patented devices according to literature data. There were no statistically significant differences between the two study groups: the average AF value in the first group was 0.87 [0.86, 0.89], in the second – 0.86 [0.80, 0.89]. In both groups, there was a significant correlation of AF with age ($p < 0.05$, $R = 0.6$). AF intensity was increased with age over 30 years in patients with diabetes, but not in healthy individuals. In type 1 diabetic patients AF correlated with CKD ($p=0,01$), albumin-creatinine ratio ($p=0,04$). AF also correlated, although not statistically

significant, with A1C (p=0,06), diabetes duration (p=0,07), average daily glucose level (p=0,07), creatinine in blood (0,07). No correlations were observed between AF values and diabetic retinopathy, neuropathy, glycemic variability. This may be due to the small number of patients in the study sample and requires further research.

Conclusions. The results obtained using the FOS-1 coincide with those obtained using certified analyzers AGEs, which indicates the possibility of using the described method for the control of disorders of carbohydrate metabolism, as an early noninvasive diagnostics of renal microvascular lesions in patients with type 1diabetes.

POTENTIAL ARRYTHMOGENIC MECHANISMS OF SUDDEN CARDIAC DEATH IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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Sudden cardiac death (SCD) claims 340 000 lives per annum, making it the leading cause of cardiovascular related deaths in the United States. Obstructive sleep apnea (OSA) raises the risk of SCD up to 4 times, depending on the severity of OSA. However published reports set the association between OSA and SCD but not mechanisms of SCD. It is well known that OSA leads to repetitive nocturnal hypoxemia (NH). Notably, the severity of NH may be an independently of other well-established risk factors of SCD and strongly predict it. Hypoventilation is the most common reason of increasing PaCO2 level and acid-base disturbance initiated by an increase in PaCO2. Chronic one-night hypercapnia includes an increase in hydrogen protons at cells with decreasing intracellular potassium level via bicarbonate buffer activation. Action potential (AP) length, both at nodal tissues and ventricular Purkinje/myocardium, being electrolyte sensitive, elongates due to potassium deficit and delayed repolarization. The novel finding potassium channels expression to be inhibited rateably to OSA severity. The result is decrease repolarization reserve. This, phase 3 of the AP, is relative refractory period, during which a new stimulus such as a ventricular extrasystole can trigger arrhythmia. Hypoxemia, with associated hypercapnia, results with increased sympathetic tone, automaticity and conduction velocity and result in ventricular ectopy. Tachycardia, due to increased serum catecholamines, leads to increased myocardial oxygen demand, myocardial ischemia and ischemia-driven ventricular arrhythmias. These mechanisms should encourage OSA treatment in order to prevent SCD.

PREVALENCE OF CARDIOMETABOLIC RISK FACTORS IN RUSSIAN CARDIOLOGISTS DEPENDING ON GENDER

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Objective: The aim of the study was to compare prevalence of cardiometabolic risk factors in cardiologists who participated in Russian National congress of Cardiology 2016 depending on gender. Physicians, cardiologists are the most informed group of people regarding the cardiovascular diseases risk factors and the possibilities of prevention.

Methods: 342 doctors were screened during Russian National congress of Cardiology 2016 which took place in Ekaterinburg (Russian Federation) on September 20-23, 2016. All subjects were interviewed with special questionnaire, which included personal data, life style risk factors and medical history. Blood pressure (BP) was measured on right arm in the sitting position after 5-minute rest by automatic tonometer OMRON (Japan). Blood cholesterol and glucoses were measured by EasyTouch® GCHb (Taiwan). Anthropometry was performed according to standard procedure.

Results: Mean age was 43,2±11,6 in men and 47,0±11,7 in women and differed significantly depending on gender (p=0,01). Waist circumference was 91,5±13,9 cm in men and 25,8±5,0 cm in women (p=0,0006). Body mass index did not differ significantly: 27,2±4,9 kg/m^2 in men vs 25,8±5,0 kg/m^2 in women. With regard to blood pressure, the systolic blood pressure was significantly higher in men: 129,7±15,4 mm Hg vs 122,8±16,3 mm Hg in women (0,001). Diastolic blood pressure did not differ significantly: 81,8±10,9 mm Hg in men vs 79,7±10,2 mm Hg in women.

Cholesterol and glucose levels were 4,99±1,21 and 5,09±0,98 mmol/l in men; 5,10±1,31 and 5,07±1,40 mmol/l in women, respectively, and did not differ significantly depending on gender.

Walk (minutes per week) was 317±309 in men vs 311±272 in women and did not differ significantly. Sleep (hours per day) was 4,6±4,7 in men vs 3,2±3,1 in women, without significant differences. Sugary (spoons (slices) per day) consumption had significant differences: 4,6±4,7 in men vs 3,2±3,1 in women (p=0,002).

Conclusions: Despite younger age, men have a greater higher systolic pressure. The rest of the metabolic profile was comparable between males and females in spite of higher sugar intake in females.

PREVALENCE OF FAMILIAL HYPERCHOLESTEROLEMIA IN AN ADULT POPULATION OF A HIGH-CARDIOVASCULAR RISK COUNTRY – INSIDES FROM XTEND SURVEY

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OBJECTIVES

The estimate the prevalence of familial hypercholesterolemia Romanian adult population.

METHODS

A representative sample of 1523 adults (mean age 51.14±16.23 years, age range 18-80 years, 55.7% females) were enrolled in XTEND national representative survey after signing a written informed consent. The evaluation of each enrolled subjects included: completion of the study questionnaire that included the Dutch Lipid Clinic Network (DLCN) diagnostic criteria for familial hypercholesterolemia (FH), anthropometric measurements, 3 sitting BP measurements at 1 minute interval (Omron M6AC, adjusted cuff for arm circumference) and serum lipids evaluation using capillary blood using Cobas b 101 devices. Definite FH was defined by a DLCN >8 points, probable FH by a DLCN of 6 – 8points, possible Familial Hypercholesterolemia by a DLCN score of 3 – 5 points and unlikely FH by a DLCN score <3 points.

RESULTS

Mean values of lipids recorded were: total cholesterol: 197.11±46.26mg/dl, triglycerides: 188.51±108.82mg/dl; LDL-cholesterol: 102.96±40.73mg/dl, HDL-cholesterol 57.46±19.52mg/dl. Mean DLCN score was 1.20 points, range: 0-16 points. Definite FH was recorded in 1.5% of the study sample, while probable FH was recorded in 2.4% and possible FH was recorded in 14.9%. Subjects with definite FH were in their majority hypertensives – 62.3%, in 35% obese, only half of them were receiving hypolimnion treatment but all of them had abnormal lipid values.

CONCLUSIONS

The preliminary results of XTEND survey reveals that 1 out of 70 Romanian adults have familial hypercholesterolemia, with a low hypolipemiant treatment rate and lack of adequate control, frequently associating other CV risk factors, having therefore a high risk of severe CV events.

PREVALENCE OF OBESITY AMONG THE FACULTY OF SAINT PETERSBURG UNIVERSITIES

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Purpose: The aim of the study was to assess of the prevalence of obesity in the faculty members of Saint Petersburg universities. This subpopulation is well-educated and can affect lifestyle attitudes of students.

Methods: This cross-sectional study was conducted in October to December 2016 and comprised 866 professors of six Saint Petersburg Universities, aged 22-80 years. The informed consent was obtained from all participants. Anthropometric measurements of weight and height were taken with all participants wearing light clothes and no shoes according to standard procedures. Body Mass Index (BMI) was calculated in kg/m^2 by dividing weight (in kg) by the square of the height (in meters). Waist circumference (WC) was measured above the iliac crest and below the lowest rib margin at minimum respiration. Overweight was defined as BMI ≥ 25 kg /m^2 and < 30 kg/m^2 and obesity as BMI ≥ 30 kg/m^2. Subjects were determined as being obese when WC≥ 94 cm in males and ≥80 cm in females according to International Diabetes Federation (IDF) recommendations.

Results: Mean age of participants was 53,1±11,2 years. There were more female participants (74%) in the study. The average BMI was 26,9±4,7 kg/m^2 with significant gender differences: BMI for males was higher 27,6±3,8 kg/m^2 compare to females was 26,6±5,0 kg/m^2 (p=0,004). Overweight was detected significantly more often in males 53,5% comparing with females 33,5%. Obesity according to BMI was detected in 22,7% of the participants (22,1% in males and 22,9% in females, p>0,05). Abdominal obesity defined by WC was revealed in 61,8% of the individuals (62,0% in males and 61,8% in females respectively, p>0,05). The prevalence obesity according to both criteria (BMI and WC) was 70,1% (78,3% and 67,2% in males and females respectively, p<0,05).

Conclusion: Our study demonstrated high prevalence of obesity among university professors of St. Petersburg – until 70% according to both criteria. The prevalence of overweight and obesity determined combined by BMI and WC was significantly higher in males.

PREVALENCE OF THE CARDIOVASCULAR DISEASES RISK FACTORS IN PATIENTS WITH AORTIC STENOSIS

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The aim of this study was to analyze the occurrence of the major risk factors for CVD in pts with aortic stenosis.

Materials and Methods: We performed analysis of the database of 13802 patients who were observed and underwent echocardiography at the North-West Federal Medical Research Centre (Vivid 7, GE). We included patients with age>18 years and peak aortic jet velocity (Vmax) > 2.0m/s.

Results: Aortic stenosis was identified in 909 patients (6.6%). Overall, 381 (42%) were men and 528 (58%) were women, with a mean age of 66.01±12.1 years. All patients were divided into 2 groups: 764 patients (84%) with tricuspid aortic valve (TAV) and 145 patients (16.0%) with bicuspid valve (BAV).

Patients with TAV were significantly older than BAV patients (69.0 ± 9.9 years vs 50.6 ± 19.9 years, p<0.001). Hypertension was observed in 683 patients (89.4%) with TAV and in 89 patients (61.4%) with BAV, p<0.001. Prevalence of diabetes in TAV and BAV patients was 234 (30.6%) and 27 (18.6%), p<0.01. There were no differences in the obese occurrence in TAV and BAV patients (253 (33.1%) patients vs 36 patients (24.8%), p<0.22). Prevalence of smoking was significantly higher in BAV then in TAV patients: 40 patients (27.6%) vs 113 patients (14.8%), p<0.001. Family history of CVD had 200 patients (26.2%) with TAV and in 35 patients (24.1 %) with

BAV, p<0.05. History myocardial infarction was more common in TAV patients than in BAV (168 patients (22%) and 21 patients (14.5 %), p=0.03). Hypertensive and normotensive TAV and BAV patients did not differ in Vmax and there wasn't significant correlation between blood pressure level and Vmax which may be therapy related. Despite the fact that in patients with TAV mean body mass index was higher than in BAV patients (28.6±5.01 vs 26.8±4.95, p<0.01), there was no correlation of body mass index with Vmax.

Conclusions: CVD risk factors such as age, hypertension and diabetes are associated with TAV but not with BAV, that may be due to the different pathophysiological mechanisms of TAV and BAV calcification.

PREVALENCE, TREATMENT AND CONTROL OF DYSLIPIDAEMIA IN ADULT POPULATION FROM A HIGH-CARDIOVASCULAR RISK COUNTRY – PRELIMINARY RESULTS OF XTEND SURVEY

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OBJECTIVES. To estimate the prevalence, treatment, and control of dyslipidemia in adult population of Romania, a very high cardiovascular risk East European, data that has a crucial importance for the development of prevention strategies at national level

METHODS. A representative sample of 1523 adults (mean age 51.14±16.23 years, age range 18-80 years, 55.7% females), randomly selected from the GPs list activating in three territorial regions of Romania were enrolled after signing written informed consent. The evaluation of each enrolled subjects included: completion of the study questionnaire, anthropometric measurements (waist, height, neck, arm, waist and hip circumferences), 3 sitting BP measurements at 1 minute interval performed with an AAMI validated automated BP measuring device (Omron M6AC, adjusted cuff for arm circumference) and complete lipid evaluation using capillary blood and a point-of-care Cobas b 101 devices. Dyslipidemia was defined as abnormal values of at least one lipid test (total cholesterol ≥ 190mg/dl, LDL-cholesterol≥ 115mg/dl, HDL-cholesterol≤ 40mg/dl (male) and ≤ 45mg/dl (female) and triglycerides≥ 150mg/dl) or previously diagnosed condition under treatment during the last two weeks, regardless of lab values.

RESULTS. Mean values of lipids recorded were: total cholesterol: 197.11±46.26mg/dl, triglycerides: 188.51±108.82mg/dl; LDL-cholesterol: 102.96±40.73mg/dl, HDL-cholesterol 57.46±19.52mg/dl. The proportion of abnormal lipid values was: 54.4% hypercholesterolemia, 54.8% hypertriglyceridemia, 36.1% high LDL-cholesterol and 17.9% low HDLcholesterol. The general dyslipidaemia prevalence was 80.1%, in majority of the cases – 50.3% representing a newly diagnosed condition. Only half of previously diagnosed dislipidemic subjects were treated (49.9%) and a normal lipid profile was recorded in only 23.1% of the treated dislipidemic subjects.

CONCLUSIONS. The preliminary results of XTEND survey reveals that Romanian adult population is facing an epidemic of dyslipidemia with a very high prevalence especially of newly diagnosed cases, together with low treatment and control rates, that stresses the urgent need of prevention strategies at national level.

PROGNOSTIC VALUE OF DIABETES MELLITUS AND RENAL DYSFUNCTION IN THE IMPLEMENTATION OF ADVERSE OUTCOMES AT THE LONG-TERM TREATMENT STAGE IN PATIENTS WITH ST-ELEVATED MYOCARDIAL INFARCTION

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According to the data of epidemiological studies there is a tendency towards an increase in the number of patients with diabetes mellitus (DM) mainly due to an increase in the number of patients with type 2 DM. Renal injury in DM occurs in 30-60% of patients. The patients with renal dysfunction (RD) and DM refer to a category of a very high risk for cardiovascular complications. It is important to determine the role of both the isolated impact of DM and RD in the development of cardiovascular complications and their joint impact on the outcomes of acute coronary syndrome.

Purpose. We aimed to evaluate the impact of DM and RD in the implementation of adverse outcomes of the long-term treatment stage (3 years) in patients with ST-elevated myocardial infarction (STEMI).

Material and methods. The study group consisted of 954 STEMI patients admitted to the Kemerovo Cardiology Dispensary in the period 2008-2010 within 24 hours since the moment of clinical picture development. The study protocol met the requirement of the local ethics committee. The study included 620 (65%) men, median age – 60.3 [59.4-61.1] years; and 334 (35%) women, median age– 69.2 [68.1-70.4] years.

The patients were divided into 4 groups depending on the presence of RD and DM: the first group included patients with DM and RD, the second group – patients with DM and without RD, the third group – patients with DM and with the reduced GFR, the fourth group – without DM and with the preserved renal function.

Among the total number of patients included into the study, 112 (11.7%) died at the hospital stage and 70 (8.35%) – within a year after discharge. Three years after STEMI the information on the status of 7 patients couldn't be obtained. Thus, in 3 (36+-2 months) years after STEMI the prognosis was estimated in 761 (79.8%) patients in the comparison groups:in the first group of patients with DM and RD (n=51, 39.5%), in the second group (n=78, 60.5%), in the third – without carbohydrate metabolism disorder (CMD) and withRD (n=189, 29.9%) and in the fourth− withoutDM and with GFR> 60 ml/min/1.73 m^2 (n=443, 70.1%).

The verification of STEMI diagnosis was performed on the basis of clinical, biochemical, electrocardiographic and echocardiographic characteristics of this disease (Society of cardiology of the Russian Federation, 2007). The presence of DM was established on the basis of anamnesis data, analysis of outpatient cards, indicators of oral glucose tolerance test (WHO, 1999). All the patients were assessed for blood serum creatinine level on admission and on day 12 of hospitalization with the estimation of glomerular filtration rate (GFR) using CKD-EPI formula (2009). RD was diagnosed in GFR less than 60 ml/min/1.73 m^2.

Results and discussion. The analysis of the long-term outcomes during 3 years of observation after STEMI showed the significance of the combination of RD and DM for the formation of adverse outcome. The greatest number of deaths was noted in the group of patients with DM and RD – 2.6 times more than in the group of patients without DM and with the preserved renal function (15.69 vs 6.09%, p=0.0001); 2 times more than in the group with DM and without RD (15.69 vs 7.69%, p=0.0001); and 1.7 times more than in the group with DM and without CMD (15.69 vs 8.99 %, p=0.0001).

When comparing the isolated impact of DM or RD on the prognosis of STEMI patients during 3 years of observation a great amount of deaths was noted in the group with the presence of RD and without CMD as compared to the group of patients with DM and preserved renal function (8.99% vs 7.69%, p=0.0001, χ^2=62.66).

The data of univariate analysis indicates 2.5 times increased risk of death during the three-year period after STEMI inpresence of RD (OR 2.5, 95% CI 1.7-3.6, p=0.0001); 2.3 times–in the history of MI (OR 2.3, 95% CI

1.5-3.4, p=0.0001), 3.8 times–in patients' age over 60 years (OR 3.8, 95% CI2.5-5.7, p=0.0001) and1.8 times–in presence of DM (OR 1.8, 95% CI1.1-2.7, p=0.009).

Using the multivariate logistic regression we revealed aset of predictors significantly affecting the possibility of fatal outcome in patients within three years after STEMI. A significant impact of age over 60 years (OR 2.1, 95% CI 1.1-3.9, p=0.003), the presence of MI history (OR 1.9, 95% CI 1.1-3.7, p=0.001) and RD (OR 1.4, 95% CI 1.2-1.6, p=0.04) revealed on the acute period of MI, were demonstrated.

Conclusion. Renal dysfunction has a significant impact on the implementation of adverse outcomes in STEMI patients with underlying DM, moreover, the great prognostic value of the combination of DM with RD, as well as the isolated renal function impairment for the development of adverse outcomes in long-term treatment stage of STEMI was proved.

QUALITY OF LIFE IN PATIENTS WITH PANCREATIC CANCER WITH AND WITHOUT METABOLIC SYNDROME

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Aim: To compare the quality of life (QOL) in patients with pancreatic cancer (PC) with and without metabolic syndrome (MS).

Materials and Methods: 33 patients with PC were examined (20 persons without MS – group 1; 13 persons – with MS – group 2). The groups were comparable to sex and age. From each patient provided written informed consent to participate in the study. PC diagnosis was confirmed by histology, for MS classification used classification of NCEP ATP III (2004). QoL was assessed by questionnaire «SF-36». Statistical analysis was performed using SPSS software (11.0).

Results: In patients 1 and 2 groups of QOL indices did not differ significantly according to the following scales of the questionnaire: physical role functioning (RF) 9,3±5,1 balls (b) and 14,3±4,3 b, p>0,05; physical pain (BP) 44,4±7,3 b and 49,6±8,5 b, p>0,05; general health (GH) 32,2±6,8 b and 35,9±7,1 b, p>0,05; social functioning (SF) 31,9±6,4 b and 34,1±6,7 b, p>0,05; role-emotional functioning (RE) 11,7±5,6 b and 14,8±6,2 b, p>0,05; mental health (MH) 57,7±6,3 b and 60,7±7,9 b, p>0,05. In Group 2 patients showed a significant improvement in quality of life on the scale of the vitality (VT) 43,6±4,8 b and 56,5±5,7 b, p<0,05 and physical functioning (PF) 46,2±5, 8 b and 61,8±6,7 b, p<0,05 compared with group 1 patients.

Conclusions: The patients with PC without MS QoL indices do not differ on the most scales of the SF-36 questionnaire (RF, BP, GH, SF, RE, PH), compared with patients with PC with MS. At the same time in PC patients without MS QoL significantly worse on scales PF and VT than in patients with PC with MS that can probably be explained by a lesser severity of physical pain.

RESULTS OF VIDEOOESOPHAGOGASRODUODENOSCOPY AT HIGH RISK STROKE PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION

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Objective. Atrial fibrillation (AF) is the most prevalent sustained arrhythmia in clinical practice associated with increased risk of stroke and systemic thromboembolism. Oral anticoagulants reduce the risk of stroke and mortality in AF patients but increase the risk of bleedings. The most common bleedings in AF patients treated with oral anticoagulants are nasal or gastrointestinal (GI).

Aim of the study. To evaluate the significance of videooesophagogastroduodenoscopy (VEGDS) in non-valvular atrial fibrillation patients with absolute indications to oral anticoagulation therapy.

Materials and methods. Case histories of 1882 patients hospitalized in cardiology and internal medicine departments of university clinic in 2016 and 129 results of VEGDS of AF patients with absolute indication for oral anticoagulation therapy were analyzed.

Results. Among 1882 hospitalized persons 263 patients had non-valvular AF, 253 of them (96,2%) had ≥1 (males) or ≥2 (females) clinical risk factors for stroke or systemic embolism according to CHA2DS2-VASc score. Anticoagulation therapy was absolutely indicated to 240 AF patients (91,3%) – CHA2DS2-VASc ≥2 (males) and ≥3 (females). Anticoagulation therapy was recommended to 211 patients (88%), other patients had contraindications or refused to take this medications.

VEGDS is not obligatory test before starting anticoagulation therapy and thus, was performed only at 115 AF patients. In 50 patients (43,5%) pathology of oesofagus, stomac and duodenum, predisposing to upper GI bleedings, was diagnosed, while only 17 of them (34%) had high risk of bleeding (≥3 points of HAS-BLED score).

Among patients with pathologic changes of upper GI tract 71,4% had erosive gastritis or duodenitis, 5,5% – gastric or duodenal ulcers, 3,5% – gastrooesophageal reflux disease with erosions, 1,6% – cancer of oesophagus, 18% patients had combined pathology. Frequency of GI pathology predisposing to GI bleedings did not differ from patient's age – 46% among those who were younger than 75 years and 40% among patients 75 years and older. Ion-deficient hypochromic anemia was diagnosed in 23 AF patients (46%) with abnormal VEGDS and 20 AF patients (31%) with normal VEGDS. Only 11 (22%) patients with GI pathology had symptoms of gastric dyspepsia, burning et al.

Conclusions. Prophylactic videooesophagogastroduodenoscopy reveals asymptomatic pathology predisposing to upper gastrointestinal bleedings. We hope that diagnosing and treatment of these diseases before starting anticoagulation therapy will reduce gastrointestinal bleedings in patients with non-valvular atrial fibrillation and high risk of stroke and systemic embolism.

RISK FACTORS OF CARDIOVASCULAR DISEASES – COMPONENTS OF METABOLIC SYNDROME IN RUSSIA AND CHINA

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Objective. Components of metabolic syndrome (MS) are well known risk factors of cardiovascular diseases (CVD) and epidemiology of these risk factors is very important prognostic value of CVD.

Purpose of the study. To compare epidemiology of cardiovascular risk factors – components of metabolic syndrome in Russia and China.

Materials and methods. In Russia we chose Multicenter observation study ECVD-RF (Epidemiology of Cardiovascular Diseases and their Risk Factors in Regions of Russian Federation) – risk factors of CVD were evaluated in 11 regions in 18305 persons 25-64 years old in the period 2012-2013 years (1). In China CVD risk factors were studied in 2010-2012 years among 104098 adults from 31 regions of China according to metabolic syndrome criteria of CDS (Chinese Diabetes Society) (2).

Results. In China crude prevalence of MS was 15,4%; in Russia MS prevalence is absent in this publication. Obesity (BMI≥25.0 kg/m2) in China – 32,3%, in Russia (BMI≥30.0 kg/m2) – 29,7±0,3%. High glucose level (FPG≥6.1mmol/L and/or OGTT-2h≥7.8mmol/L) in China – 16,2%, in Russia (FPG≥7.0 mmol/L or diabetes) was diagnosed in 4,6±0,2%. Arterial hypertension (BP≥140/90 mm Hg) was evaluated in 22,4% in China and in 33,8±0,4% persons in Russia. High level of total cholesterol was revealed in 57,6±0,4% in Russia. In China dyslipidemia was diagnosed in 33,7% persons, high level of triglycerides – in 23,7%, low level of high density lipoprotein cholesterol – in 20,8%.

Conclusions. To compare results of national epidemiologic studies is difficult due to different parameters and its different abnormal criteria used by investigators. Epidemiology of arterial hypertension is more wide in Russia among adults – 33,8% than in China – 22,4%. Epidemiologic trials should be continued.

RISK OF ADVERSE DRUG EFFECTS IN PATIENTS WITH DIABETES MELLITUS DEPENDING ON THE PRESENCE OF IHD

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Objective. To assess the risk of adverse drug effects (ADE) in patients with diabetes mellitus type II (DM II) depending on the presence of ischemic heart disease (IHD).

Material and methods of investigation. The hospital histories of 66 patients with DM II (average age 66.1 ± 9.0 years) who was hospitalizated to the hospital for 3 months of 2017 were involved in the analysis by method of continuous reading. The GerontoNet score was used to assess the risk of ADE. All patients were divided into 2 groups, depending on the presence of proven diagnosis of IHD. The group of patients with DM II without IHD included 24 patients, 54.2% of women, the average age of 62.2 ± 8.6 years. The second group included 42 patients with DM II and IHD – 54.8% of women, the average age of 68.3 ± 8.5 years.

Results of the study. The average number of cardiovascular diseases (CVD) in patients with DM II without IHD was 1.5 ± 0.6, which is significantly less than in group DM II / IHD (3.7 ± 1.4, $p < 0.05$). The concomitant non- cardiovascular diseases are 3.1 ± 1.3 and 4.7 ± 2.4, respectively, $p < 0.05$. The incidence of atrial fibrillation in the group without IHD was 4.2%; in the group DM II / IHD – 31.0% ($p < 0.05$). All patients had arterial hypertension, and more than 60% of patients had 3 degrees. Obesity was more often recorded in the group without IHD (83.3% vs. 57.1%, $p < 0.05$). The level of total cholesterol and LDL was comparable – 5.4 ± 1.2 mmol/l and 4.9 ± 1.1 mmol / l; 3.8 ± 1.2 and 3.0 ± 0.9. The target level of LDL in the groups had 4.2-4.8% of patients taking atorvastatin 40 mg. The target level of glycated hemoglobin was in the majority of patients (68.4% and 81.0%). The glomerular filtration rate less than 60 was in 8.3-14.3% of patients; albuminuria was recorded in 16.7% of cases. In the examination, significant angiostenosis of brachiocephalic vessels were detected in 25-21.4% of hospitalized patients. Semeiotic CHF with saved left ventricular ejection fraction was established in 1.3% of patients with DM II without IHD and in 50% of DM II/ IHD.

The number of the prescribed drugs in the hospital was 5.7 ± 1.6 in DM II group and 7.6 ± 1.8 in the DM II/ IHD group. The average number of points on the GerontoNet score was 1.7 ± 1.0 and 4.0 ± 1.9, respectively, $p < 0.05$. In the group of patients with DM II/ IHD 2.4% of them have a very high risk of ADE (8 points for GerontoNet), high risk (6-7 points) – 21.4% of patients. In the group DM II without IHD the risk of ADE was less than 10%.

Conclusion. The combination of DM II and IHD leads to a significant increase in concomitant cardiological and noncardiological conditions, for which reason patients are forced to receive more drugs, which increases the risk of ADE, especially in old age.

ROSUVASTATIN DOSE-DEPENDENTLY IMPROVES FLOW-MEDIATED DILATION, BUT REDUCES ADIPONECTIN LEVELS AND INSULIN SENSITIVITY IN HYPERCHOLESTEROLEMIC PATIENTS

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Background: Increased risk of type 2 diabetes noted with statins is at least partially explained by HMG-coenzyme A reductase inhibition. We investigated vascular and metabolic phenotypes of different dosages of rosuvastatin in hypercholesterolemic patients.

Methods: This was a randomized, single-blind, placebo-controlled, parallel study. Age, sex, and BMI were matched among groups. Forty-eight patients were given placebo, and 47, 48, and 47 patients given rosuvastatin 5,10, and 20 mg, respectively daily during a 2 month treatment period.

Results: Rosuvastatin 5,10, and 20 mg dose-dependently and significantly improved flow-mediated dilation (34, 40, and 46%) after 2 months therapy when compared with baseline ($P<0.001$ by paired t-test) or when compared with

placebo (P<0.001 by ANOVA), and increased insulin (median % changes; 16, 20, and 20%, respectively) and glycated hemoglobin levels (mean % changes; 2, 2, and 3%, respectively), and decreased adiponectin levels (mean % changes; 3, 9, and 14%, respectively) and insulin sensitivity (mean % changes; 2, 3, and 4%, respectively) after 2 months therapy when compared with either baseline (all P<0.05 by paired t-test), or when compared with placebo (P=0.006 for insulin, P=0.012 for glycated hemoglobin, P=0.007 for adiponectin, and P=0.002 for insulin sensitivity by ANOVA).

Conclusions: Rosuvastatin treatment dose-dependently and significantly resulted in decreasing insulin sensitivity and increasing ambient glycemia by reducing adiponectin levels and increasing insulin levels in hypercholesterolemic patients.

SCORING SYSTEM FOR OBSTRUCTIVE SLEEP APNEA SYNDROME IN MEN WITH NEWLY DIAGNOSED ARTERIAL HYPERTENSION

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Introduction. Arterial hypertension (AH) is one of the diagnostic criteria for the obstructive sleep apnea syndrome (OSAS). This condition is more often diagnosed in men. Data on some features of the course of arterial hypertension with OSAS are accumulated.

Objective: To determine the predictors of OSAS based on ambulatory blood pressure monitoring (ABPM) in men with newly diagnosed AH.

Material and methods: 197 men (mean age 40.1 ± 8.4 years) with newly diagnosed AH mild (62.9%), moderate (25.9%), severe (11.2%) degree. 156 (79.2%) patients were diagnosed with OSAS. The control group consisted of 31 men – without AH and OSAS. A study was conducted: clinical, laboratory and instrumental methods, Epworth scale of daytime sleepiness. Diagnosis of OSAS and ABPM monitoring were performed on a portable multifunctional recorder ('Kardiotekhnika-07', Incart, St. Petersburg, Russia). OSAS was diagnosed at apnea-hypopnea index (5 or more per 1 hour of sleep). The duration of sleep was determined from the actigraphy data. Predictors of the presence of OSAS studied on 32 parameters: age, anthropometric data, night cardiorespiratory test and ABPM, values of heart rate. Statistical analysis of the results was carried out using descriptive statistics, correlation and regression analysis and ROC analysis (receiver operating characteristic).

Results. Patients with obesity (mean body mass index 34.4 ± 5.0 kg/m^2), neck circumference 40 cm and more (96%) and dyslipidemia (65.5%) prevailed in the sample. Positive response to the question of snoring was answered by 82%, about smoking – 33%. The averaged value of the total score according to the Epworth scale of daytime sleepiness is 7.8 ± 4.8 points. OSAS of moderate and severe degree (apnea-hypopnea index 15 and more per 1 hour of sleep) was diagnosed in 100 (51.7%) patients. The four predictors of OSAS are defined, for each the odds ratio is calculated: body mass index (1.13, 95% CI 1.05-1.22, p < 0.002), hypoxemia index (1.12, 95% CI 1.06-1.18, p < 0.000), time indices in sleep for diastolic blood pressure (1.03, 95% CI 1.01-1.04, p < 0.002) and systolic blood pressure (0.99, 95% CI 0.98-1, 00; p < 0.045). The scoring system for OSAS was created, the sensitivity of the test is 76.0%, the specificity is 77.8%. This model generated a ROC with an area under the curve of 0.848.

Conclusion. To the predictors of OSAS in men with newly diagnosed AH are body mass index and the index of hypoxemia, as well as those obtained with ABPM – time index, calculated for the period of sleep for diastolic and systolic blood pressure.

SERUM LEPTIN LEVELS IN VERY ELDERLY PATIENTS WITH CORONARY ARTERY DISEASE

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Introduction

Very limited data are available on leptin in very elderly patients. Therefore, we evaluated serum leptin levels and their relationship with obesity and other disorders in patients with coronary artery disease (CAD).

Methods

Serum leptin levels were measured in 90 hospitalized patients (females – 65.5%, males – 34.5%) with CAD. The mean age of patients was 88.3±4.3 years (from 75 to 98 years). Normal ranges for serum leptin levels in women were 3.6-11.1 ng/ml, in men – 2.0-5.6 ng/ml. Fat mass was assessed by the dual-energy X-ray absorptiometry.

Results

Mean leptin concentration in the study group was 17.2 (0.49-100) ng/ml. 60% of patients had increased leptin levels. Serum leptin levels in women were 2.3 times higher than in men; increased concentrations were detected in 67.7% of women and in 45% of men ($p=0.03$). Decrease of leptin concentration was registered in 14.4% of patients; all but one of these had severe heart failure. Serum leptin levels were strongly correlated with body mass index ($p<0.0001$). Significant positive correlations between serum leptin and fat mass were revealed: $p=0.0001$ – for total fat, $p=0.002$ – for abdominal fat, $p=0.004$ – for upper extremities fat, $p=0.003$ – for lower extremities fat. Leptin levels were positively correlated with total cholesterol and triglycerides concentrations ($p=0.0002$). Higher leptin levels were observed in patients with diabetes mellitus (21.01 vs 16.26 ng/ml, $p=0.06$); increased leptin was associated with higher glucose level ($p=0.004$). There was a trend to higher leptin levels in patients with atrial fibrillation (19.3 vs 14.6 ng/ml, $p=0.2$)

Key conclusions

Study results demonstrated high prevalence of leptin abnormalities in very elderly patients with CAD. High leptin levels are associated with increased fat mass. Serum leptin levels are strongly correlated with various disorders.

SIGNIFICANT DIFFERENTIAL VASCULAR AND METABOLIC EFFECTS OF SIMVASTATIN COMBINED WITH EZETIMIBE AND SIMVASTATIN ALONE IN PATIENTS WITH HYPERCHOLESTEROLEMIA

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Background: Vascular and metabolic effects of simvastatin combined with ezetimibe have not been investigated in patients with hypercholesterolemia, compared with simvastatin alone.

Methods: This was a randomized, single-blind, placebo-controlled, parallel study. Fifty-one in each group were given placebo, ezetimibe 10 mg combined with simvastatin 10 mg (Vyto10), ezetimibe 10 mg combined with simvastatin 20 mg (Vyto20), or simvastatin 20 mg alone (Sim20), respectively daily for 2 months.

Results: Placebo therapy did not significantly change insulin and insulin sensitivity (determined by QUICKI) and adiponectin levels and visceral fat and visceral fat/subcutaneous fat (V/S fat) ratio relative to baseline measurements. Vyto10 therapy significantly decreased CRP and insulin levels and increased adiponectin levels and insulin sensitivity, and reduced visceral fat, V/S fat ratio, and blood pressure relative to baseline measurements. Vyto20 therapy did not significantly change insulin levels and insulin sensitivity and adiponectin levels but sig-

nificantly reduced CRP levels and visceral fat, V/S fat ratio, and blood pressure relative to baseline measurements. Sim20 therapy significantly decreased adiponectin levels and insulin sensitivity but did not significantly change visceral fat, V/S fat ratio, and blood pressure relative to baseline measurements. Of note, these different effects of each therapy on CRP, insulin, adiponectin, insulin sensitivity, and blood pressure were significant by ANOVA.

Conclusions: Vyto10, Vyto20, and Sim20 showed significantly differential vascular and metabolic effects.

SPECIFICS OF CARDIOGEMODYNAMICS IN PATIENTS WITH ISCHEMIC DILIATION CARDIOMYOPATHY AND OBESITY

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Objective: to assess the role of obesity in the formation of myocardial architectonics in patients with ischemic dilated cardiomyopathy.

Materials and methods: the work was based on the results of clinical and instrumental studies in 58 men with ischemic dilated cardiomyopathy (the final diastolic size of the left ventricle 60 mm and more) without signs of decompensation at the time of examination. The first group included 27 patients with normal and increased body weight. The second group consists of 31 patients with different degrees of obesity. The study did not include persons in need of valve replacement (valves) in decompensated state. On the first day of the examination, all patients performed a six-minute walk test, electrocardiography and echocardiography according to a standard procedure, lipidogram study and fasting blood glucose level.

Results: in terms of body mass index (BMI), the patients of the first group were distributed as follows: in 28% of cases, BMI was within the normal range, and increased body weight was found in 72% of cases. Patients of the second group in 43% of cases had obesity of 1 degree, 28.5% – obesity of the 2nd degree and 28.5% – obesity of the third degree. Average waist measurements exceeded the recommended values (94 cm), in both groups, which indicated the presence of abdominal obesity. In the second group, this index was 121.3 ± 8.5 cm, which is 19.16% higher than in the control ($p < 0.05$). For the ejection fraction, the patients were distributed as follows: in the 1st 21% of patients had a low ejection fraction, 43% had an average, and 36% had a preserved fraction. In the 2nd group, 28% had a low ejection fraction, 28% had an average fraction, and 44% had a preserved fraction. When assessing cardiohemodynamic parameters in obese patients, the size of the left atrium was 13.9% higher than in patients with normal body weight ($p < 0.05$). The thickness of the interventricular septum was 20%, and the back side was 18.64% larger in the group of patients with obesity than in the control group. The left ventricular myocardial mass index exceeded the values in the group of obese patients by 9.38% compared with the control ($p < 0.05$). In the group with obesity, the diastolic dysfunction E / A was 36.36% higher than in the control group ($p < 0.05$). The ejection fraction in the obese group was 6.8% lower than in the control ($p < 0.05$). It should be noted that the size of the left and right ventricles was not significantly different between the groups.

Conclusions: the structure of the heart in patients with ischemic dilated cardiomyopathy has its own characteristics, depending on the presence of obesity. In patients with obesity, more severe left ventricular hypertrophy is observed, accompanied by a more pronounced diastolic left ventricular dysfunction, and as a result – a greater degree of dilatation of the left atrium and a lower ejection fraction. Consequently, obesity is an additional pathogenetic factor, weighting the course of ischemic dilated cardiomyopathy.

STRESS HYPERGLYCEMIA IN ACUTE MYOCARDIAL INFARCTION AND RISK OF TYPE 2 DIABETES MELLITUS

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Background. Stress hyperglycemia (SH) in non-diabetic patients with acute myocardial infarction (AMI) is demonstrated to be a predictor of adverse outcomes. Association of SH with newly diagnosed glucose metabolism disorders (GMD) after AMI is controversive.

Purpose. The purpose was to evaluate the association between SH in AMI and the risk of type 2 diabetes mellitus (DM) in postinfarction period and long-term follow-up period (during 1 year after AMI).

Methods. We consecutively included 52 patients 44 to 73 years of age, with first-ever AMI, Killip class I-II, treated with percutaneous transluminal angioplasty. The exclusion criteria were: GMD diagnosed before or during hospitalization (HbA1c≥6.5%), severe concomitant diseases, taking glucocorticosteroids. All the patients had history of hypertension and received β-blockers, antihypertensive therapy, desaggregants, statins. We conducted a prospective study. Plasma glucose (PG) was measured on admission, fasting PG was measured on the 5-10th day of hospitalization. SH was defined as admission PG is more than 7.8 mmol/l, normoglycemia was defined as admission PG is less than 7.8 mmol/l and fasting PG is less than 6.1 mmol/l. Plasma lipids level weight, height were measured during hospitalization, body mass index (BMI) was calculated as body mass (kg) divided by height (m) squared. HbA1c was measured during hospitalization or before 3 months after discharge to exclude previously undiagnosed DM. Standard oral glucose tolerance test with 75 g of glucose was conducted and HbA1c was measured 2–6 months after AMI and the testing was repeated 1 year after AMI in 30 patients. In the absence of unequivocal hyperglycemia the results were confirmed by repeat testing a week later. We compared the results between patients with SH and normoglycemia. Differences in continuous and categorical variables were compared by the Mann-Whitney U-test and the exact Fisher's test respectively.

Results. The range of admission glucose values was 4.8-13.7 mmol/l. There were 24 hyperglycemic and 28 normoglycemic patients. The groups were comparable by clinical, demographic and biochemical parameters. Mean age was 61.0 (55.0;66.0) and 59.5 (55.0;64.0) years, mean BMI was 27.9 (25.4;30.3) and 27.9 (25.1;32.5), high density lipoprotein cholesterol level was 1.02 (0.80;1.27) and 1.03 (0.75;1.12) mmol/l, triglyceride level – 1.69 (1.22;2.60) and 1.73 (1.44;2.85) mmol/l respectively. In postinfarction period the incidence of newly diagnosed type 2 DM was 20.8% and 7.1% respectively (p=0.227). The incidence of DM during a 1 year follow-up was significantly higher in the group with SH (58.3% vs 11.1%, p=0.013).

Conclusions. SH in AMI is associated with higher incidence of newly diagnosed type 2 DM in a long-term follow-up period.

THE ANALYSIS OF INITIAL CHANGES IN LIPID AND CARBOHYDRATE METABOLISM IN THE EXPERIMENT

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It is well-known that long-acting stimuli, such as deprivation or excessive consumption of fat food cause of tension adaptive mechanisms. Thus, they can promote the development of metabolic discords and may lead to cardiovascular diseases (dyslipidemia, diabetes, obesity). To identify the primary disorders in the lipid and carbohydrate metabolism, models in a few species of experimental animals are used. The purpose of this study was to define and estimate the initial effects of: 1) caused by sensory and social deprivation in dogs, 2) the chronic feeding of experimental rodent animals with a high-calorie diet, for changes in parameters of lipid and carbohydrate me-

tabolism. In conditions of psychosomatic stress (deprivation) caused by fool isolation from communication with relatives in dogs-males raised from 3 weeks to 10 months of age were determined. The experienced dogs differed with the destructive type of behaviour, some disturbances of normal brain function, as well as increased blood levels of corticosteroids from control animals. It was found that in complete isolated dogs compared to the control individuals in the blood plasma, a higher level of total cholesterol (CH), triglycerides (TG) and phospholipids was observed at 29%, 27% and 24%, respectively. It should be emphasized that after 7 months of isolation, the neurosis-like state that developed in complete isolated dogs complicated the process of elaborating conditioned reflexes and was accompanied by an increase (by 1.5 times) in the concentration of glucose (Gl) in the blood of these animals. The content of Gl in the control group of dogs under these conditions significantly decreased. The results suggest that prolonged isolation of young animals leads to a change not only in their behaviour and hormone levels, but also causes initial disturbances of lipid and carbohydrate metabolism. Excess intake of food enriched with saturated fats is a risk factor for obesity, but also for dyslipidemia due to the accumulation of total CH and TG in the blood and liver. To simulate alimentary dyslipidemia (DLP), experimental animals (guinea pigs, 450-500 g) were kept for 30 days on a high fat diet with an excessive content of food exogenous cholesterol (as an imposed nutritional load). The high fat diet for guinea pigs consisted of 2% XC and 40% fat mix (pork lard/sunflower oil 3:1). By the end of the experiment the body weight of the experimental animals receiving diet increased by 27%. Chronic alimentary DLP in guinea pigs was characterized by an increase in lipid levels in the blood and liver. Thus, the concentration of total CH and TG in serum increased 4.7 and 6 times, respectively, and the level of HDL cholesterol decreased 4-fold. In the liver we can see a pronounced accumulation of lipids (total CH and TG) too. The obtained results indicate, that excessive consumption of food enriched with saturated fats and exogenous cholesterol for experimental animals, susceptible to development of DLP promotes initial disturbances of lipid metabolism in guinea pigs. It was suggested that these experimental models are useful for screening new pharmacological agents of the metabolic type of action.

THE EXPERIENCE OF USING A NEW METABOLIC ACTION OF L-DOPA

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Neurotropic drug L-DOPA (Dopaflex, Levopa) as the «gold standard» is used to treat Parkinson's disease in significant doses (5-10 g/ per day) sufficiently long time. However, you can see many severe complications which limited prolonged application of this drug. Previously, in patients with coronary heart disease (CHD), the ability of L-DOPA in small doses to stimulate reparative processes, restore the activity of the sympathetic adrenal system and reduce the progression of lipid peroxidation was established in joint experimental and clinical studies. Materials and methods. In this investigation, the results of the complex application of L-DOPA as a metabolic corrector are demonstrated. A clinical study in 43 elderly men (59-67 years) with CHD complicated by dyslipoproteinemia (DLP) and severe arterial hypertension (AH) (blood pressure 160/90 mm Hg) were carried out. These patients were divided in two groups: 1-control (20 men) receiving baseline (standard) therapy, and 2-experimantal group (23 men) receiving baseline (standard) therapy with adding Levopa (1.5 g, 4 weeks). Baseline (standard) therapy was concluded of the complex of famous antihypertensive therapy and drugs against angina pectoris. All parameters of blood were determined by biochemical analyzer with the certificated methods.

Results. In the experimental group (23 men) with DLP and AH after the basic course of therapy and L-DOPA (in a dose of 0.5 g 3 times a day), normalization of blood pressure and improvement of the lipid spectrum of blood, as well as a number of metabolic parameters, were observed. In the blood plasma of patients receiving L-DOPA in addition to standard therapy, the level of total cholesterol, low-density lipoprotein cholesterol, triglycerides and atherosclerotic coefficient were lowed in blood significantly. We observed the decrease in the concentrations of hormone corticosterone, glucose and peroxide products in blood plasma. Compared with the standard treatment of CHD only, there was an early improvement in overall well-being and good mood in the experimental group of patients.

Conclusion. Thus, in this short clinical study, an antiparkinsonian Levopa drug in small doses has a pronounced hypolipidemic and metabolic effects.

THE FTO RS9939609 POLYMORPHISM IN PATIENTS WITH ABDOMINAL OBESITY

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Objective. To evaluate serum lipid profile in patients with abdominal obesity carrying FTO variants (rs9939609 polymorphism).

Methods. The study involved 149 patients (59 men and 90 women) with abdominal obesity (AO) (IDF, 2005) aged 30 to 55 (the average age was 46.2±6.9 years) and residing in Saint-Petersburg. The control group consisted of 87 apparently healthy people (30 men and 57 women) without AO. Serum lipid profiles were measured by enzymatic techniques (COBAS INTEGRA 400/700/800 reagents, Germany). DNA was quantified by Real-Time PCR method (Applied Biosystems, Foster City, CA), and the TaqMan SNP genotyping technique (TaqMan® SNP Genotyping Assay, Human SM) was used to identify the rs9939609 polymorphism of the FTO gene.

Results. Comparison of genotype distribution showed no significant difference between the group of patients with AO and the control group of apparently healthy people (TA – 48.32% and 55.17%; TT – 32.21% and 29.89%; AA – 19.46% and 14.94%, respectively; $p>0.05$). Allele frequencies in subjects with AO and the controls were also not significantly different (A allele – 0.4362 and 0.4253, respectively; $p>0.05$). In patients, A-allele carriers had higher levels of total cholesterol than carriers of the TT-genotype, (5.69±0.11 mmol/L and 5.3±0.17 mmol/L, respectively; $p<0.05$). Patients with AO carrying various genotypes rs9939609 of the gene of interest had similar levels of high density lipoprotein, low density lipoprotein, triglycerides (1.24±0.04 mmol/L and 1.25±0.07 mmol/L; 3.62±0.11 mmol/L and 3.26±0.18 mmol/L; 1.67±0.09 mmol/L and 1.51±0.12 mmol/L, respectively; $p>0.05$).

Conclusion. Patients with abdominal obesity who carried A allele rs9939609 of the FTO gene had higher cholesterol levels than carriers of the TT genotype rs9939609 of the gene.

THE IMPACT OF OBESITY ON THE GESTATIONAL DIABETES (GD) CLINICAL FEATURES AND BIRTHWEIGHT

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Aim. To study the BMI contribution into the GD course, birthweight

Design and methods. The prospective study included 41 age-matched patients: 1st group consisted of 26 women with GD, 2nd group – 15 healthy pregnant controls. Two subgroups were separated: non-obese women (n=19 in the 1st group) and women with obesity (n=14 in the 2nd group). BMI, GD course and birthweight were assessed ($p < 0,05$).

Results. Pre-pregnancy BMI in the 1st group was 26,18+/-8,29; in the 2nd group – 25,8+/-7,37. Obesity was diagnosed in 26,7% cases in the 1st and in 6,7% women among controls. Mean birthweight was 3613+-407g and 3353+/-567 g in the 1st and 2nd groups, respectively. Mean fasting glucose in the 1st group was 4,72+/-0,7 mmol/l (non-obese), 5,04+/-0,9 mmol/l (obesity), in the 2nd group 4,1+/-0,5 mmol/l (non-obese), 4,75+/-0,3 mmol/l (obe-

sity). At the mean GD was diagnosed significantly earlier in obese 1st group participants (11,9 +/-3,4 gestational weeks) comparing with non-obese women (21,7+/-4,2 gestational weeks). Birthweight in the non-obese 1st group participants was 3587+/-280g (3546+/-245g in good glycemic control of GD), in obese – 3675+/-303g (3610+/-215g); in the 2nd group 3310+/-234g (3307+/-242g) and 3950+/-357g in non-obese and obese patients, respectively.

Conclusion. According to our data GD in patients with obesity is characterized by more severe disease course, earlier onset and higher rate of macrosomia, however the main contributor of birthweight is supposedly the glycemic control.

THE IMPORTANCE OF VARIOUS DIAGNOSTIC METHODS OF CARBOHYDRATE METHABOLIZM DISORDERS BEFORE THE PERCUTANEOUS CORONARY INTERVENTIONS

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Introduction: carbohydrate methabolizm disorders (CMD) are a predictor of poor prognosis of coronary heart disease (CHD), as well as a risk factor for early and late complications of coronary interventions. In the routine practice, the active detection of CMD in this group of patients is not widely spread, and consequently, in some patients, the CMD remains unrecognized with no correction. In majority of cases, the diagnosis is established on the basis of fasting glycemia. It has been proved that unrecognized CMDs have a significant adverse effect on the course of IHD and the prognosis in this category of patients.

Aim: To evaluate the effectiveness of various diagnostic methods to detect CMD in patients before the planned PCI.

Materials and methods: The prospective study was started in November 2016. Inclusion criteria: verified stable CHD with the presence of indications for the planned PCI, absence of any coronary revascularization earlier. Totally 58 patients were included in the study, without previously established CMD s.

All patients underwent fasting glucose evaluation, determination of HbA1c level, and an oral glucose tolerance test. Diagnosis of CMD was carried out according to the Algorithms of specialized medical care for people with diabetes mellitus (8th edition, 2017).

Results. The mean age was 59.97 ± 6.43 years. Among 58 patients (100%) type 2 diabetes was diagnosed in 8 (13.8%) people, impaired glucose tolerance in 3 (5.17%), and fasting glycemia in 13 (22.41%) people. All patients underwent an initial fasting glycemia evaluation that allowed to detect type 2 diabetes in 5 patients (62.5% of all patients with newly diagnosed type 2 diabetes). 53 patients underwent oral glucose tolerance test, who detected 34 patients without glycemic disorders (64.15% of all), an additional 3 patients with type 2 diabetes mellitus (5.66% of all oral glucose tolerance test and 5.17% of all examined), 3 patients with impairment glucose tolerance and 13 patients with impaired fasting glycemia (24.53% of all oral glucose tolerance test and 22.4% of all subjects). In summary, when actively diagnostics, newly detected CMDs were registered in 24 people (41.28% of 53 patients with oral glucose tolerance test). In 3 (12.5%) patients with newly diagnosed CMDs (for the first time in 24 people), the level of plasma glycemia was less than 6.1 mmol/l).

Conclusion. In routine practice, the diagnosis of CMD in patients with coronary artery disease and indications for planned coronary revascularization is often based only on data on the evaluation of glycemia and is inadequate. Oral glucose tolerance test performance allows to identify more than 40% of persons with a history of CMD s, and, consequently, to develop a set of measures for prevention of early and late complications.

THE INCIDENCE OF NONALCOHOLIC FATTY LIVER DISEASE AND DYSLIPIDEMIA IN PATIENTS WITH ARTERIAL HYPERTENSION DEPENDING ON THE PRESENCE AND SEVERITY OF OBESITY

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The purpose of the study: to study the incidence of nonalcoholic fatty liver disease and dyslipidemia in patients with primary arterial hypertension depending on the presence and severity of obesity.

The research material. There were 52 patients with arterial hypertension of 2 and 3 stages. Depending on the magnitude of the body mass index the patients were divided into subgroups. The first comprised 12 patients without obesity (mean age 65.8 years); the second in 10 patients with excessive body mass (mean age 69 years); the third 18 persons with the first degree of obesity, the fourth of 12 patients with grade 2 obesity (mean age 63.6 years) and five of 12 people with the third degree of obesity (mean age 62 years).

Research methods. Types of dyslipidemia was established according to the criteria of classification of dyslipidemias WOS. Index of steatosis liver (ISL) was calculated according to the formula Lee Jeong-Hoon et al. (2010). To determine the severity of liver fibrosis were used Bonacini discriminant counting scale. The obtained data were correlated with the stage of fibrosis by METAVIR scale (O. N. Mikushkin, 2012).

The results of the study. Patients depending on the severity of obesity there has been an increase of ISL. So, at the first degree of obesity, in contrast to the group with overweight, the ISL was higher by 37.1%, in the second degree, in contrast to the group with the first degree of obesity, by 4.2%, from the third degree of obesity, in contrast to the group with the second degree of obesity at 17.8%. All of them were diagnosed fibrosis of the liver, corresponding to stages F0-F1 by METAVIR classification. Thus the smallest discriminant score on the scale was in the third degree of obesity (1.3 times less than in persons with excess body weight, 10% less than in individuals with a first degree and 14.2% than in individuals with the second degree of obesity).

The presence of dyslipidemia in individuals without obesity were detected in 49.9 %, with excess body weight in 60%, with the first degree of obesity in 77,7%, in 66.6%, third degree – in 66.6%.

In individuals without obesity 33.3% identified dyslipidemia 2A, 16.7% of type 4; with excess body mass: 20% identified dyslipidemia 2A, 40% dyslipidemia 4; at the first degree of obesity: in 44.4% identified dyslipidemia 2A, 11.1 percent dyslipidemia 2B and in 22.2% dyslipidemia 4 types. At the second degree of obesity in 66.6% of dislipidemia was revealed 4 types in the third degree: 33.3% dyslipidemia 2B, 33.3% of dyslipidemia 4.

While steatosis is diagnosed in individuals without obesity in 16.6%, and steatohepatitis in 16.6%; overweight – 20% of identified steatohepatitis; at the first degree of obesity at 11.1% steatohepatitis, 88.8% of steatosis; the second degree of obesity – 33.3% – steatosis, 66.6% of steatohepatitis, with the third – 100% steatosis.

Thus, depending on the obesity increases the ISL and the frequency of occurrence of hepatic steatosis, however, the linear dependence of the frequency of steatohepatitis and the severity of liver fibrosis have not been identified. In individuals without obesity, with overweight and with the first degree of obesity prevalent dyslipidemia 2A; the second and third – dyslipidemia 4 and 2B.

THE PATHOGENETIC ROLE OF OBESITY IN THE PROGRESSION OF ATRIAL FIBRILLATION IN PATIENTS WITH METABOLIC SYNDROME

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Objective: to determine anthropometric predictors of progression of atrial fibrillation (AF) in patients with metabolic syndrome (MS).

Materials and methods: 86 patients with MS with paroxysmal (PAR) and permanent (PER) forms of AF were examined. All patients underwent calculation of body mass index (BMI), measurement of waist and hip volume, echocardioscopy (E) by standard method, electrocardiography in 12 standard leads, fasting blood glucose level, lipidogram. Patients with signs of dilatation of the left ventricle (end diastolic size 60 mm and above) according to E and cardiovascular events in the history did not enter into the work. Metabolic syndrome diagnosis was established according to the new criteria of the International Diabetes Association.

Results: all examined patients had central obesity. The waist circumference (WC) in men with PAR AF was 107.15 ± 10.06 cm, in men with PER AF 107.73 ± 12.52 cm. In women with PAR AF 106.69 ± 13.53 cm, with PER AF 113.91 ± 16.51 cm. Thus, WC exceeded the recommended values, respectively, in PAR and PER AF in men at 13, 99 and 14.61% , while in women at 33.36% and 42.39% ($p<0.05$).

According to the BMI, men with PAR AF and PER AF did not differ (30.19 ± 5.78 kg/m^2 and 31.11 ± 6.32 kg/m^2, respectively). In men with PAR AF, the excess body weight was found in 59.25%, the first degree of obesity in 29.63%, the II degree of obesity in 3.7%, the third degree in 7.42%. In men with PER AF, normal body weight was determined at 11.76%, and excess in 35.28%. Obesity of the 1st degree is revealed in 29.43%, II degree in 17,65%, III degree in 5,88% of cases.

The mean BMI in women was 32.93 ± 6.46 kg/m^2 and 35.42 ± 7.17 kg/m^2, respectively, with PAR and PER AF. According to the BMI with PAR AF, the distribution was as follows: normal body weight was detected in 10%, increased in 23.33%. Obesity of the I degree is revealed in 23.33%, II degree in 23.33%, III degree in 20% of cases.

The mean BMI in women was 32.93 ± 6.46 kg/m^2 and 35.42 ± 7.17 kg/m^2, respectively, with PAR and PER AF. According to the BMI with PAR AF, the distribution was as follows: normal body weight was detected in 10%, increased in 23.33%. Obesity of the I degree is revealed in 23,33%, II degree in 23,33%, III degree in 20% of cases. Among the patients with PER AF, 33.33% had an increased body weight. Obesity of the 1st degree was detected in 25%, II degree in 16.67%, III degree in 25%. In men with PAR and PER AF, obese patients were 40.74% and 52.93%, respectively. In women with PAR and PER AF, different degrees of obesity were found with the same frequency at 66.66%.

Probably, obesity contributed to the development and progression of AF in the studied group of women.

According to the recommendations of the ESH / ESSC 2013, the left ventricular myocardial mass index (LVMI) more than 115 g / m^2 in men and more than 95 g / m^2 in women is the criterion of asymptomatic myocardial damage in hypertension.

LVMI in men with PAR AF exceeded the recommended indices by 26.95%, and with PER AF by 29.58% ($p<0.05$). The women with PAR AF BMI exceeded the recommended indicators by 54.72%, and with PER AF by 50.41% ($p<0.05$).

The following data were obtained in the analysis of the incidence of asymptomatic myocardial damage. LVMI exceeded normal values in 85.19% in men with PAR AF and 88.24% in men with PER AF. In women with PAR and PER AF, LVMI was higher than normal in 96.67% and 100% of cases, respectively. Thus, in women, asymptomatic myocardial damage was more common than in men by 11.48% in PAR AF and 11.76% with PER AF ($p<0.05$).

Conclusions: Different rates of obesity were more frequent in women than in men, 1.64 times in PAR AF and 1.23 times in PER AF ($p<0.05$). Abdominal obesity also was more pronounced in women with metabolic syndrome and AF. Obesity was an additional factor in the development of left ventricular hypertrophy and subsequent AF in women with metabolic syndrome along with hypertension.

THE PREVALENCE OF ANXIETY AND DEPRESSION IN DISPENSARY PATIENTS WITH CHRONIC HEART FAILURE

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The steady increase in the incidence and mortality of chronic heart failure (CHF) in part of the reason may be related to the increase in the number of patients with psycho-emotional disorders. A total of 50 patients with coronary heart disease (CHD) and CHF were examined under the dispensary supervision of the city polyclinic in Voronezh. Using psychometric scales of anxiety and depression (Spielberger-Khanin and Tsung, respectively), the study determined that disorders of anxiety-depressive spectrum in ambulatory patients with CHF have a high prevalence. Surveyed 94% of patients suffered from depression, 74% of patients had a high level of personal anxiety, 56% of patients had high level of anxiety. Gender differences depended on the presence of CHF: in the absence of CHF and more susceptible to depression were female, and the group of patients with CHF and depression in men were found much more often in women with coronary artery disease without signs of heart failure. Personal anxiety in CHD patients with CHF were more pronounced in comparison with the group of CHD patients without CHF. The frequency of occurrence of trait anxiety among patients with CHF amounted to 91.3%. A high level of personal anxiety was more frequently found in men, in situational women. Timely detection and correction of anxiety and depression in outpatients are the key to successful management of patients with CHF and increases patient compliance to treatment.

THE RESULTS OF STUDYING THE FREQUENCY OF OCCURRENCE OF SYMPTOMS OF GASTROESOPHAGEAL REFLUX DISEASE IN PATIENTS WITH COMBINED CARDIOVASCULAR PATHOLOGY AND DIABETES MELLITUS TYPE 2

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The purpose of the study. To study the incidence of gastroesophageal reflux disease (GERD) in patients with associated heart pathology on the background of abdominal obesity of the first degree of diabetes of the second type.

Material and methods. Surveyed 30 women with arterial hypertension (AH) stage 3 and coronary artery disease, exertional angina FC 1-2 and abdominal obesity 1 degree. The group was divided into subgroups. The first consisted of 15 people with diabetes type II diabetes (mean age 72 years), the second 15 people without diabetes (mean age 74 years).

Was used questionnaire GerdQ for diagnostics of gastroesophageal reflux disease (GERD) and scale the most common symptoms of GERD (Frequncy Scale for Symptoms of GERD, FSSG), which was evaluated by the total score of symptoms associated with reflux and dysmotility of the esophagus.

The results of the study. In the first group group, unlike the second, it was observed lower values for the total score on questionnaire GerdQ 18.7% ($p<0.05$). The value of the score for the questions of group A (which indicates the presence of symptoms, evidence in favor of GERD, i.e. the presence of heartburn and regurgitation) in the first group were 2.7 times ($p<0.05$) below. The average score on questions in groups B (which puts the diagnosis of GERD is questioned) in the first group 23.9% higher ($p<0.05$), and average score for the questions in group C (showing the effects of the disease on quality of life) 27.3% ($p<0.05$) less than in the second group. In the first group, 80% there is a low probability of GERD, 20% – severe. In the second group, a low probability detected in 40% of individuals and 60% – severe.

According to the scale value of the FSSG total score in the first group 2.2 times less ($p<0.05$), the magnitude of scores that reflect symptoms associated with reflux in 2.2 times less ($p<0.05$) and the magnitude of the symptoms reflecting infringement of a motility of the esophagus is 2.8 times less ($p<0.05$) than in the second group.

Conclusions. Thus, this study demonstrated that the use of scales for identification of GERD in individuals with diabetes is ineffective little or asymptomatic gastroesophageal flow disease in this group of individuals and requires focused inquiry.

THE RISK OF ACUTE ATHEROGENIC DISEASES IN GENERAL POPULATION WITH VITAL EXHAUSTION IN RUSSIA/SIBERIA: GENDER FEATURES. WHO PROGRAM MONICA-PSYCHOSOCIAL

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Objective: To determine the influence of gender differences in vital exhaustion (VE) on the risk of myocardial infarction and stroke in a general population aged 25–64 years in Russia/Siberia.

Methods: In frame of the third screening WHO program «MONICA-psychosocial» a random representative sample of the population aged 25-64 in Novosibirsk in 1994 (men n = 657, women n = 870) was surveyed. The program included: registration of socio – demographic data; identification VE. Over 16-year period cases of MI and stroke incidence in women (15 and 35) and men (30 and 22) were identified, respectively. Cox regression model was used for relative risk assessment (HR).

Results: VE level were: men 66.8% (-14.6% high), 75.7% in women (44.4% higher). The risk of MI among men with VE was HR =2. We did not get the effect of VE on the risk MI among women. RR of MI in persons with VE were higher among divorced women HR = 5.4, than men HR = 4.7. Risk MI was higher in men with VE: primary education HR = 2.2; have never married HR = 3.7, widowed male HR = 7, in 45-54 years HR = 3.8 and HR = 55-64 5.9. In women, these associations have been identified. Risk of stroke in patients with VE were higher in women HR = 3.34, than men HR=3.1. Risk stroke was higher only in men with VE: with incomplete secondary – primary education HR = 4.8; men, divorced HR = 3.8, widowed men at HR = 3.6. Risk of stroke among people older than 55 years was higher in women HR = 2.9, than men HR = 2.4.

Conclusion: Prevalence of VE was higher in women than in men. Vital exhaustion is a predictor of MI in men and stroke in both genders.

THE STUDY OF INFLUENCE OF INFLAMMATORY MEDIATORS ON EA.HY926 MONOLAYERS PERMEABILITY FOR LIPOPROTEINS

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Increasing permeability of endothelial monolayer of large arteries is a key step in atherogenesis which promotes accumulation of low density lipoproteins (LDL) in intima. Mechanisms of such dysfunction of endothelium are not well understood. This study was focused on evaluation of effects of inflammatory mediators CRP and TNFa on endothelium permeability for lipoproteins and some other human plasma proteins. For doing this, we applied the model of confluent HUVEC hybridoma EA.Hy926 cell line grown on collagen-covered porous chambers. Isolated LDL, albumin or human serum were added to culture mediums in upper wells of chambers and in specific time intervals (1-24h) the aliquots of media from low wells were taken for ELISA analysis of apolipoproteins (apo) B, A-1, albumin and IgM content. The permeability, or transport rate, was calculated as % ratio of proteins content in low chambers to the amount added.

Incubation of monolayers with 200 mkg/ml CRP stimulated transport of both apolipoproteins at 12h, while for IgM and albumin it was achieved only at 24h. The effect of TNFa (50 ng/ml) was more specific, since in 24h it increased permeability for apo B but not for albumin. In lower time intervals there were not found any significant

effects of mediators studied on transport. To evaluate whether CRP or TNFa increased endothelium permeability for lipoproteins through activation of clathrin we added to monolayers clathrin inhibitor aminazine. Aminazine suppressed LDL and albumin uptake but had no effects on basal transport of these molecules through endothelium monolayer though abrogated CRP stimulated transport of apo B.

Results of this study show late responses of EA.Hy926 cell line on inflammatory stimuli and some of their effects could be mediated through activation of clathrin-coated vesicles. This cell line could be further applied as a model for further investigation of mechanisms of increasing endothelial permeability in atherosclerosis.

TYPE 2 DIABETES IN ACUTE CORONARY SYNDROME AND ACUTE MYOCARDIAL INFARCTION (FRAGMENT OF THE RESEARCH «RACSMI-UZ»)

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Objective: To assess the effect of type 2 diabetes mellitus (DM 2t) on the clinical course in patients with acute coronary syndrome and acute myocardial infarction (a fragment of the Research «RACSMI-Uz»).

Material and methods: 417 patients hospitalized in the hospitals of the experimental district of Tashkent were included in this fragment of the study (229 men (54.9%) and women (188%)). Out of 417 patients, 83 (19.9%) suffered from DM 2t. Criterion for the presence of diabetes in the history was the indication of the patient himself for the available diabetes or medical documents (extracts from outpatient cards or case histories), confirming the presence of such. All patients were: history taking, according to the protocol of the ACS / MI registry; Physical examination; General clinical laboratory studies (determination of lipid spectrum and biochemical blood test). Statistical processing of the data was carried out using the Statistica 6.0 application package.

Results: Mean age of respondents with DM 2t. was 60.1 ± 7.3 years; the age of men being younger than women (58.7 ± 7.5 years and 61.5 ± 7.0 years, respectively, $p > 0.05$). An analysis of the complaints showed that the most frequent noted the chest pain of varying degree – 72 (86.7%), weakness – 70 (84.3%) and dyspnea – 66 (79.5%) cases. Cold sweat was recorded in 13 (15.7%) patients, and the asymptomatic form of ACS / MI was detected only in 5 (6.1%) people. In 2 (2.4%) cases, ACS / MI was recorded as syncope.

During the analysis of the anamnestic data, it was found that almost 70% of the patients had burdened on CHD heredity, in addition more than 40% of patients already had postinfarction cardiosclerosis (PICS), while only 19.3% had percutaneous interventions (PCI) or Aortocoronary bypass grafting (CABG). Complications, such as chronic heart or renal failure, were present in 64% and 18% of patients, respectively. Attention is drawn to the fact that 46% of patients had a hereditary anamnesis on the development of DM 2t.

Conclusions: The occurrence of type 2 diabetes among persons with ACS / MI, according to the data of the register «RACSMI-Uz», was 20%. The most typical complaints for ACS / MI in individuals with type 2 diabetes were pain in the chest, weakness and dyspnea, the occurrence of which was 80%, while asymptomatic disease was observed in 6% of patients. Weighed IHD heredity was detected in 70% of the examined patients, while 40% of the patients were characterized by myocardial infarction, but only 19% of patients underwent these or other types of surgical interventions. Weighed heredity for type 2 diabetes was found in 46% of the examined.

VARIANTS WITHIN THE APOB, PCSK9 AND SORT-1 PLAY A ROLE IN PSEUDO-FH DEVELOPMENT IN CZECH POPULATION

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Aim: Familial hypercholesterolemia (FH) is a serious disease, leading (if not treated) to premature myocardial infarction. FH is caused predominantly by mutations within the *LDL receptor* and *APOB* genes. Recently, gene score from 12 SNPs within different genes have been defined, suggesting the existence of «pseudo-FH», clinically indistinguishable from classical FH, but without one causal mutation. In our pilot study, we have analyzed some from these SNPs in Czech patients with FH.

Methods: APOB rs1367117, PCSK9 rs24790409, NYNRIN rs8017377, SORT-1 rs629301, LDL-R rs6511720 and ABCG-8 rs4299376 variants were genotyped using TaqMan technology on an AB 7300 RT PCR cycler in 298 FH patients without the causal mutation and in 296 patients with the LDL receptor mutation.

Results: Frequencies of the individual genotypes significantly differ between two analyzed groups in the case of *APOB* ($P < 0.006$), *PCSK9* ($P < 0.05$) and *SORT-1* ($P < 0.05$), but nor for *NYNRIN* ($P = 0.41$), *LDL-R* ($P = 0.97$) or *ABCG-8* ($P = 0.15$) genes.

Conclusion: The results from our pilot study underline the importance of some common genetic variants in the «pseudo-FH» development. Analysis of *APOB*, *PCSK9, SORT-1* SNPs (and very likely some others) is necessary to complete the real genetic causality of «FH» in patients without the detected mutation.

VASCULAR REMODELING IN PATIENTS WITH ACUTE CORONARY SYNDROME WITHOUT ST ELEVATION AFTER STENTING WITH STENTS WITH A BIODEGRADABLE DRUG COATING

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Introduction: Diseases of the circulatory system are currently one of the leading causes of disability and mortality in Russia. Significant contribution to the structure of morbidity and mortality is caused by ischemic heart disease.

Nowadays, methods of myocardial revascularization have been developed, such as coronary artery stenting, improving the quality of life and the patient's prognosis. However, after stenting, the patient can develop restenosis and acute coronary thrombosis. To reduce the risk of these complications, new stents with a biodegradable drug coating have been developed.

Purpose: To assess the degree of healing after stenting with a biodegradable drug eluting stents

Materials and methods: The study included 10 patients aged 50 to 70 years admitted to the clinic due to the development of an acute coronary syndrome without ST elevation, which was used to install a biodegradable drug eluting stent. After 4 months, these patients underwent repeated coronarography in combination with optical coherence tomography to evaluate the healing score. All patients received dual antiplatelet therapy and statin therapy.

Results: During the study, 4 patients underwent repeated coronarography in combination with optical coherence tomography. In all patients, complete coverage of the stent with an unintentional stent is noted, in the presence of stent deformations, single uncovered strats were noted. One patient stented simultaneously with drug eluted stent and bare metal stents (BMS) noted restenosis of BMS stents with adequate neoepithelization of a stent with a biodegradable drug coating.

Conclusion: Initial data suggest that biodegradable drug eluted stents have a lower risk of restenosis than uncoated stent, and a lower risk of early coronary thrombosis, given the extent of neointimal coverage. Futher investigation should prove this data.

VITAMIN D DEFICIENCY AS RISK FACTOR OF THE METABOLIC SYNDROME: 3-YEAR PROSPEKTIVE STUDY

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Objective(s). Vitamin D deficiency could be a risk factor of metabolic disorders. The aim of study was to assess the contribution of vitamin D deficiency into the metabolic syndrome (MS) development in females.

Materials and methods. A total of 469 women St. Petersburg residents from 30 to 55 y.o. were examined. Serum 25(OH)D level was determined by chemiluminescent method, using lab kits for Abbott Architect 8000 (USA). Endocrine Society (2011) vitamin D deficiency criteria were applied. Initially and in 3-year follow-up MS components availability (International Diabetic Federation (IDF), 2005) criteria were assessed in 70 women.

Results. The study results showed that only 44 (9,4%) women had normal vitamin D status, 425 (90,6%) women were insufficient (30,3%) or deficient (60,3%). In 70 women examined in 3 years the initial serum 25(OH)D level was between 10,0 to 66,0 nmol/l (mean 50,4±5,9 nmol/l). Basal body mass index (BMI) was 31,2±0,8 kg/m^2 (from 26,1 to 39,9 kg/m^2), waist circumference (WC) value was 96,1±1,8 cm. Prevalence of abdominal obesity (AO) was 94,3%, dyslipidemia – 30,0%, impaired glucose tolerance or type 2 diabetes – 68,6%. The blood pressure (BP) level was within normal values. Among females with vitamin D deficiency was a larger quantity with reduced HDL cholesterol level, than in normal serum 25(OH)D level ($p<0,05$). The 3-year follow-up mean values of IMT, WC, BP, serum 25(OH)D, glucose and lipids levels did not differ from initial data ($p>0,05$). We found that number of women with reduced HDL cholesterol level increased after 3-year period ($p=0,05$), while the number of females with AO, hyperglycemia, hypertriglyceridemia, and high BP did not change ($p>0,05$). Negative HDL cholesterol level dynamic was directly associated with WC value dynamic ($p<0,05$). Linear regression analysis showed close association between WC and HDL cholesterol level ($R^2=0,1$, $p<0,01$), as well as HDL cholesterol level dynamic ($R^2=0,1$, $p<0,05$). However basal vitamin D status was not associated with prevalence of MS in 3 years.

Conclusions. The 3-year prospective study results showed, that occurrence of AO, hypertension, impaired glucose tolerance and hypertriglyceridemia, as well as MS were not interlink with initial serum 25(OH)D level. Within, females with vitamin D deficiency had often decreased HDL level than vitamin D sufficient subjects at beginning of study, but HDL level dynamic was correlated with WC value only. These findings need to performed more longer follow-up studies.

FEATURES OF METABOLIC DISORDERS IN WOMEN WITH PERIPHERAL ARTERIAL DISEASE

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Metabolic disorders affect the course of peripheral arterial disease (PAD), which is reflected in the results of surgical interventions in this category of patients(women).

The aim of the research is to determine the metabolic status of women with atherosclerotic lesions of peripheral arteries for preparation for surgical interventions.

MATERIALS AND METHODS: A total of 331 patients with atherosclerotic lesions of lower limb arteries (2b-4 cf., Fontein-Pokrovsky classification) were examined. Patients were divided into 2 groups by gender: 135 female patients composed the main group, 196 male patients composed the control group. We analyzed the severity of carbohydrate and lipid disorders, hemodynamic parameters, and the frequency of concomitant pathology.

Statistical processing was performed using "STATISTICA-10" software package. The value «p <0.05» is indicated as statistically significant. The odds assessment was calculated using univariate analysis.

Results: Diabetes mellitus and increased blood glucose level were more often noted in female patients (6.9 ± 2.1 v/s 6.1 ± 1.2 mmol/L, or median, 25% -75%: 6.6, 5.9-7.2 v/s 6.1, 5.4-6.4, p <0.05). The value of glycated hemoglobin, as an indicator of decompensated diabetes mellitus, was higher in women (13.7 ± 3.7% or median, 25% -75%: 10.3, 8.2-19.9) than in men (7,6 ± 2.7% or median, 25% -75%: 6.4, 6.1-8.0, p <0.05). The atherogenic coefficient was higher in women (5.9 ± 1.5 v/s 4.7 ± 1.3, or median, 25% -75%: 4.8, 3.5-6.4 v/s 4.6, 4.1-5.8 p <0.05). Arterial hypertension and obesity were more often recorded in women (p <0.05). Concomitant heart failure was more often noted in female patients (p <0.05). Women tend to have chronic kidney disease more often.

Conclusion: The high severity of metabolic disorders in women suggests a more careful implementation of corrective measures in the preoperative period.

STATUS OF VEGETATIVE REGULATION IN PATIENTS WITH HYPERTENSION ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA

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The purpose of research – to study the parameters of heart rate variability (HRV) in patients with arterial hypertension (AH) and obstructive sleep apnea.

Materials and methods. To achieve this goal in the Republican Specialized Scientific-Practical Center of Therapy and Rehabilitation named after Semashko 45 patients with hypertension I-II degree were examined, including 29 men and 16 women aged 36-61 years, mean age (53,4 ± 2.3). Verification of the diagnosis was carried out on the basis of the WHO classification / ISH (1999) and PMC-VI. In addition to traditional measurements of blood pressure, all patients underwent echocardiography and night monitoring saturation of arterial hemoglobin oxygen (to diagnose obstructive sleep apnea syndrome) using a portable pulse oximeter «HandHeld Patient Monitor» (China). In this case, assessment was made for the presence of apnea episodes – cessation of breathing for 10 seconds or more of hypopnea – reduction of not less than 50% oronazal flow and / or thoracoabdominal movements involving decrease of blood oxygen saturation stored in respiratory muscle movements.

All patients were divided into 2 groups. Group 1 consisted of 20 patients with hypertensive patients with I-II degree, and group 2 of 25 patients with hypertension I-II degree with obstructive sleep apnea syndrome (OSAS).

System «Cardio Sens» was used for registration and analysis of ECG (electrocardiography). To evaluate heart rate variability performance time and frequency analysis of heart rate variability were used.

Results: At the analysis of heart rate variability in the group I it was found inhibition of parasympathetic part of the autonomic nervous system and increased activity of the sympathetic nervous system, manifesting rNN50 decrease (p <0,01), RMSSD (p <0,05), HRV TI (p <0.05); HF (p <0,01) increase and LF / HF ratio unlike the group of patients with arterial hypertension. These changes took place against the background of a moderate decline in the overall heart rate variability, as evidenced by the decrease of SDNN (p <0.05) and TR (p <0.05). Patients of group II were characterized by a greater reduction of heart rate variability. The most significant of them in relation to the group I were: mRR, SDANN, SDNN, RMSSD, LF and VLF. In a comparative analysis of heart rate variability parameters in patients of groups 1 and 11 were found to decrease LF with a tendency to LF / HF normalization of relations, as well as reduced SDNN. Patients with hypertension and obstructive sleep apnea are characterized by

further progressive reduction in most indicators of heart rate variability. All indicators except SDNNi, HF ULF were statistically significantly lower than the figures in group 1.

Conclusions: The development of the syndrome of obstructive sleep apnoe in patients with hypertension is accompanied by a decrease in the overall heart rate variability. In patients with hypertension without obstructive sleep apnea decrease in overall heart rate variability is accompanied by a decrease in the tone of the parasympathetic division. The combination of hypertension with obstructive sleep apnea syndrome is characterized by a more pronounced decrease of heart rate variability.

AMINO ACID PROFILE, HOMOARGININE AND OTHER BASIC AMINO ACID DERIVATIVES IN PATIENTS WITH LEFT VENTRICULAR DEFECTS

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Background: The aim of this study was to evaluate and compare some well-known and recently discovered metabolic markers of mitochondrial and endothelial dysfunction. The amino acid profile and endogenous amino acid derivatives, i.e., homoarginine (hArg), trimethyl-L-lysine (TML), asymmetric and symmetric dimethyl-L-arginine (ADMA and SDMA, resp.) were assessed.

Methods: We have studied plasma samples from 133 patients, including 86 cases of thoracic aortic aneurysms (TAA) 47 cases of aortic stenosis (AS) and 64 healthy blood donors. Plasma hArg, TML, ADMA, SDMA and amino acids concentrations were measured using high performance liquid chromatography.

Results: The patients exhibited only minimal shifts in routine laboratory test markers. All patients, regardless of diagnosis, demonstrated a reduction in hArg and TML, accompanied by an increase in ADMA and SDMA concentrations as compared to healthy individuals ($p<0.001$). These changes correlated with increased lactic acid concentrations in all patients ($p<0.001$). The lowest TML and hArg levels were found in TAA patients (comparing with AS group $p=0.05$ and $p=0.002$ resp.,). The changes in the amino acid profiles of the patients included significantly increased levels of Ser, Ala, Arg, and Lys.

Conclusion: The observed changes may be explained by impaired utilization of mitochondrial substrates. The independent markers of mitochondrial and endothelial dysfunction demonstrated a significant shift in patients with AS and even more pronounced changes in patients with TAA. Trimethyl-L-lysine, a known carnitine precursor, may possibly contribute to impaired fatty acid transport, causing mitochondrial dysfunction development in these patients

PREVALENCE OF ATHEROGENIC DYSLIPIDEMIA IN PATIENTS AT HIGH CARDIOVASCULAR RISK

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Background. Treatment with statins reduces the rate of cardiovascular events in high cardiovascular risk patients, but residual risk persists. At least part of that risk may be attributable to atherogenic dyslipidemia characterized by raised triglycerides and decreased levels of HDLc, driven by VLDL overproduction as a consequence of insulin resistance or hyperinsulinemia conditions.

The aim of this study was to determine the prevalence of atherogenic dyslipidemia and the accomplishment of lipidic therapeutic goals in a Spanish cohort of patients with ischemic heart disease.

Materials and Methods. A total of 78 patients with documented ischemic heart disease were included. We assessed anthropometrical, lipid and metabolic parameters. Atherogenic dyslipidemia was defined as having the following cardiometabolic disorders: HDLc<40 mg/dl (men)/<45 mg/dl (women) and triglycerides ≥150mg/dl. The accomplishment of lipidic therapeutic goals was determined by applying the "2016 ESC/EAS Guidelines for the Management of Dyslipidaemias".

Results. Atherogenic dyslipidemia was present in 28.2% of patients. The percentage of diabetic patients was 59% and it was distributed similarly between the atherogenic dyslipidemia and the non atherogenic dyslipidemia groups (63.6% vs 57.1%, p=0.600, respectively). The use of hypolipemic drugs such as statins (67.9% vs 63.6%, p=0.722) and ezetimibe (7.0% vs 9.1%, p=0.771) was similar in non atherogenic dyslipidemia and atherogenic dyslipidemia groups and we found differences in the use of fibrate (3.6% vs 22.7%, p=0.008), respectively. As expected, the atherogenic dyslipidemia group showed higher BMI (32.2±5.1 vs 29.6±4.9 Kg/m2), p=0.042), total cholesterol (202.2±57.1 vs 167.6±38.0 mg/dl, p=0.003), triglycerides (332.6±244.2 vs 104.6±53.6 mg/dl, p=0.001), apolipoprotein B (121.0±29.4 vs 89.9±23.4 mg/dl, p<0.001), non-HDLc (168.1±55.7 vs 123.3±35.7 mg/dl, p<0.001), total cholesterol/HDLc (5.98±1.69 vs 3.86±0.89, p<0.001), atherogenic index of plasma (0.916±0.250 vs 0.338±0.207, p<0.001), insulin (28.5±26.5 vs 13.4±13.5 μU/ml), HOMA index (11.4±16.1 vs 4.23±4.34, p=0.007), HbA1c (6.83±2.19 vs 6.47±1.46, p=0.044) and a trend in waist circumference (113.1±11.9 vs 105.3±16.0 cm, p=0.061) and diastolic BP (80.2±11.7 vs 75.1±9.7 mmHg, p=0.060) with respect to patients without atherogenic dyslipidemia.

In the total population, 51.5% of the patients reached therapeutic targets of LDLc <100 mg/dl, however only 10.8% achieved more stringent criteria for LDLc, <70 mg/dl. In addition, 53.8% achieved non-HDLc therapeutic targets <130 mg/dl. Specifically, the atherogenic dyslipidemia group showed similar percentage of therapeutic goals in LDLc <100 mg/dl (44.4% vs 53.6%, P=0.500) and LDLc <70mg/dl (11.1% vs 10.7%, p=0.962) with respect to patients without atherogenic dyslipidemia. In addition, patients with atherogenic dyslipidemia showed statistically significant differences in compliance with non-HDLc therapeutic goals (27.3% vs. 64.3%, p = 0.003). The presence of atherogenic dyslipidemia was associated with a higher percentage of obesity (63.6% vs 38.5%, p = 0.047), levels of visceral adiposity (89.5% vs. 60.9, p = 0.023) and non-HDLc levels> 130 (72.7% vs 35.7%, p = 0.003).

Conclusions. Patients with an ischemic disease have a prevalence of 28.2% of atherogenic dyslipidemia and a large number of these patients do not reach the therapeutic goals of LDLc and non-HDLc. Our findings support the hypothesis that atherogenic dyslipidemia shows characteristics of obesity, hypertension and insulin resistance, which in turn poses a risk of vascular complications for these patients. Specific therapeutic interventions should now be tested to address this residual risk.

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FEATURES OF CHANGES OF INSULIN RESISTANCE IN PATIENTS WITH METABOLIC SYNDROME WITH MOXONIDINE AND A COMBINATION OF MOXONIDINE WITH IVABRADINE

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AIM. To study the features of insulin resistance parameters in overweight and obese patients with metabolic syndrome treated with moxonidine and combination of moxonidine and ivabradine. METHODS. The study included 30 patients with metabolic syndrome, who were overweight (body mass index 26.9±0.2 kg/m2) and 30 patients with metabolic syndrome and obesity(BMI 34.2±0.3). Control group included 17 healthy volunteers matched with pa-

tients by age and sex. Patients with metabolic syndrome and excessive body weight received moxonidine twice daily in average daily dose of 0.58±0.07 mg. Patients with metabolic syndrome and obesity received moxonidine twice daily in average daily dose of 0.52±0.04 mg and ivabradine twice daily in average daily dose of 13.7±1.1 mg. Biochemical blood tests (insulin, C-peptide, glucose, glycated hemoglobin serum levels) were performed in all patients. RESULTS. Patients with metabolic syndrome and obesity tended to increase insulin resistance, compared to individuals with metabolic syndrome and excessive body weight. In overweight patients with metabolic syndrometreated with moxonidine, a trend for lower insulin resistance, accompanied by a decrease of insulin, C-peptide, glycosylated hemoglobin, glucose levels and homeostasis model assessment-estimated insulin resistance (HOMA-IR) index by 7.1, 2.0, 5.0, 7.3 and 12.2% respectively was discovered. Combination therapy with moxonidine and ivabradine in patients with metabolic syndrome and obesity leaded to a statistically significant improvement of insulin resistance, accompanied by a decrease of insulin levels, glucose, C-peptide, and glycated hemoglobin by 16.7%, 12.3% ($p < 0.01$); 13.2% and 10.9% ($p < 0.05$), respectively. Homeostasis model assessment-estimated insulin resistance (HOMA-IR) index decreased by 1.3 times ($p < 0.01$). **CONCLUSION.** In patients with metabolic syndrome, deepening of insulin resistance on the background of increased sympathetic activity is associated with higher grades of obesity. Combination therapy with moxonidine and ivabradine in patients with metabolic syndrome and obesity leads to a significant improvement in insulin resistance due to the additional sympatholytic effect.

SELECTIVE PPARα MODULATOR (SPPARMα): PEMAFIBRATE IMPROVED DYSLIPIDEMIA AND INCREASED HEPATOCYTE FGF21

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Background: A newly developing lipid-lowering drug Pemafibrate (PEMA; Code No. K-877) is a Selective PPARα Modulator, SPPARMα (Fruchart. Cardiovasc Diabetol. 2013). PEMA potently decreases plasma triglycerides (TG). As its key factor, Fibroblast Growth Factor 21 (FGF21) has been focused because FGF21 regulates lipid and glucose metabolisms. In this study, we report pharmacological profiles of PEMA in vitro and in vivo.

Methods: Binding of PPARα and Cofactor (CBP: CREB-binding protein) was assessed using EnBio RCAS® for PPARα Kit. Primary human hepatocytes (PHH) were stimulated by PEMA or Fenofibric acid (FA) for three days. Gene expression and protein levels of FGF21 were measured. For in vivo study, PEMA or Fenofibrate (FENO) was administered to fructose-fed rats and normal dogs for two weeks. Plasma lipids from these animals were measured.

Results: In EnBio RCAS assay, PEMA and FA stimulated the binding of PPARα and CBP in a concentration dependent manner (EC50: 3.4 nmol/L and 3297 nmol/L, respectively). In PHH, PEMA and FF increased gene expression of CPT1A, which is a common PPARα target gene. However, only PEMA increased gene expression and protein levels of FGF21 significantly. Plasma TG decreased at doses more than 0.1 mg/kg by administration of PEMA to fructose-fed rats. ED50 of PEMA and FENO were 0.14mg/kg and 21mg/kg, respectively. Administration of PEMA to normal dogs decreased plasma TG, T-CHO, and LDL-C to 68%, 26% and 54% respectively.

Conclusion: These results suggest that PEMA will be a promising drug for patients with hyperlipidemia and increase of FGF21 would be one of the mechanisms of lipid-lowering effects.

SELECTIVE PPARα MODULATOR (SPPARMα): PEMAFIBRATE IMPROVED NONALCOHOLIC STEATOHEPATITIS (NASH) IN EXPERIMENT ANIMAL MODELS

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Background: Non-alcoholic steatohepatitis (NASH) and non-alcoholic fatty liver disease (NAFLD) are kinds of the phenotypes of the metabolic syndrome. NASH is defined by the presence of steatosis coexisting with hepatic inflammation and hepatocellular injury, frequently accompanied by fibrosis. When obese and diabetic db/db mice were fed a diet deficient in methionine and choline (MCD), they develop NASH-like pathophysiology, such as steatosis, inflammation and fibrosis in liver. The present study was designed to evaluate the effects of Pemafibrate (PEMA; Code No. K-877) on NASH in the animal model.

Methods: Female db/db mice were fed MCD diet for four weeks. PEMA (0.03, 0.1 mg/kg, p.o.) or fenofibrate (FENO; 100 mg/kg, p.o.) were also administered for four weeks. Plasma lipids and parameters which participated in NASH were measured. Liver specimens were treated with Hematoxylin-Eosin stain or Masson's Trichrome stain. Typical features of NASH, e.g. steatohepatisis, inflammation, fibrosis were observed. NAFLD Activity Score (NAS) were evaluated by the method reported by Kleiner (2005).

Results: In MCD-fed db/db mice, administration of PEMA and FENO decreased plasma TG, AST and ALT.

PEMA and FENO improved the histopathological phenomena. Mean ± S.D. of NAS in MCD-fed control, 0.1 mg/kg of PEMA and 100 mg/kg of FENO-treated group were 4.9 ± 1.0, 0.9 ± 1.0 and 0.9 ± 1.4, respectively. Mean ± S.D. of fibrosis score were 1.9 ± 0.4, 0.6 ± 0.7 and 1.4 ± 0.7, respectively.

Conclusion: These results suggest PEMA would be an effective drug to treat NASH/NAFLD.

SERUM LIPID PROFILE IN VERY ELDERLY PATIENTS WITH CORONARY ARTERY DISEASE

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Background. There are few data available on serum lipids in very elderly patients with coronary artery disease (CAD); these data are conflicting.

Purpose. The purpose of this study was to determine the serum lipid profile in Russian very elderly patients with CAD as well as to evaluate its association with various disorders.

Methods. Cross sectional data from 555 hospitalized elderly patients (females – 74.5%, males – 25.5%) with CAD were analysed. The mean age of patients was 86.8+5.02 years (from 75 to 98 years). Their lipid profiles (total cholesterol (TC), high density lipoprotein (HDL-C), low density lipoprotein (LDL-C), triglycerides (TG), atherogenic index) were determined. Prevalence of hyperlipidemia was calculated.

Results. Prevalence of high serum total cholesterol and triglycerides was 13.3% and 10.4%, respectively; increase of LDL-C level was observed in 26.3% of study patients, but in the vast majority of cases hyperlipidemia was mild. Decrease of HDL-C was registered in 10.5% of patients. Significant negative correlation between TC and LDL-C concentrations and patient's age was revealed (p=0.001 for TC). Mean TC level in patients aged 75-80 years was 5.43+1.44 mmol/L; in patients 90 years of age and older – 4.7+1.08 mmol/L (p=0.001). Mean LDL-C level

in patients younger than 80 years was 3.7+1.03 mmol/L; in patients 90 years of age and older – 2.7+0.9 mmol/L (p=0.004). Females had higher concentrations of all lipids than males: mean TC level was 5.1 mmol/l vs 4.5 mmol/l in men (p<0.0001), LDL-C – 3.1 mmol/l vs 2.5 mmol/l (p=0.0002), HDL-C – 1.25 mmol/l vs 1.17 mmol/l (p=0.01). Lower lipids concentrations (mainly TC level) were significantly associated with clinically significant heart failure (p<0.0001) and atrial fibrillation (p<0.0001). Higher TC and triglycerides levels were correlated with higher blood pressure values (both systolic and diastolic) (p=0.001). Significant positive correlations between triglycerides and glucose concentration (p<0.0001) as well as between TG and uric acid level (p=0.001) were revealed. Higher triglycerides and lower HDL-C levels were registered in patients with higher creatinine level (p=0.001 and p=0.0003, respectively). In this group of very elderly patients no association was noted between lipids level and myocardial infarction and stroke in history. Only 11.4% of study patients were treated with low doses of statins.

Conclusions. The study results demonstrated some features of lipid profile in very elderly patients with CAD in comparison with well-known lipid profile of middle-aged and elderly patients. In this patient population serum lipids are strongly correlated with various disorders.

EFFECTS OF ASTHMA SEVERITY ON LIPID PLASMA LEVELS IN PATIENTS WITH ARTERIAL HYPERTENSION

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Timeliness. Arterial hypertension (AH) is one of the most common diseases nowadays. On the result of statistics, the prevalence of bronchial asthma (BA) among patients with AH is about 25-30%. According to global trends, the chronic low-grade inflammation may be the basis for the development of hypercholesterolaemia [Al-Shawwa B., 2006; Cazzola M., 2013; Scichilone N., 2013].Purpose. To study of lipid plasma levels in patients with AH and BA.

Material and methods. 73 patients with mild and the average degree (1,2 degree) of AH, associated with asthma of varying degrees in the stage of control, were involved in the study. Of them, 24 patients (33%) with AH with asthma of mild severity – group I,29 (40%) with asthma of the average severity- group II,20 (27%) – with asthma of severe degree- group III. For a comparative analysis had taken a group of 30 patients with AH of 1,2 degrees-IV group was taken for a comparative analysis. All patients received baseline treatment of BA by inhaled glucocorticosteroids (IGCS) and β2-agonists (β2-AM) short-acting. There was treatment of AH with tablet of indapamide 2.5 mg, and patients observed the recommendations about non- treatment AH therapy. Blood samples to TC, VLDL, LDL, HDL, TG were taken in all patients.

Results. In patients group III- TC 7.22 ± 1,78, VLDL-0,9 ± 0,76, LDL-3,1 ± 0,73 and TG-2,3 ± 0,91 are higher than in patients group I (TC-6,47 ± 0,93, VLDL-0,6 ± 0,51, LDL-2,2 ± 0,76 and TG-1,7 ± 0,37) and group IV (TC-6.26 ± 1,23, VLDL-0,62 ± 0,68, LDL-2,4 ± 0,87 and TG-2,1 ± 0,64), p <0.05. The level of HDL-0,96 ± 0,62 in patients of group III is lower than in studied patients group I – 1.13 ± 0.43 and group IV – 1.12 ± 0.37, p <0.05.

Conclusion. Lipid plasma levels- TC, VLDL, LDL, HDL, TG in patients with a combination of AH and BA of mild and moderate severity do not differ from those of an group with AH. Patients with AH, associated with severe BA have more higher lipid plasma level (TC, LDL, VLDL, LDL, TG) and more lower HDL level in compare to patients who have AH or AH associated with BA, mild and moderate severity.

EPICARDIAL FAT AS A PREDICTOR OF THE METABOLIC FAT OBESITY

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Epicardial fatty tissue (EFT), is a visceral fat depot (VF), which adipocytes secrets adipocytokines, taking part in the formation of inflammation, atherogenesis, insulin resistance (IR).

Purpose of the study. To study the effect of epicardial obesity (EO) on the formation of metabolic phenotypes of obesity (MFO), and to assess the prognostic significance of various obesity criteria in the formation of cardiovascular risk (CVR).

Materials and methods. The study included 110 men, 52.3 ± 3.5 years old, with arterial hypertension (AH) and the absence of clinical manifestations of atherosclerosis of any localization, type 2 diabetes. Two groups were formed, according to on the MFO for epicardial fat thickness (EFT) and body mass index (BMI). Estimation of EFT was carried out by echocardiography in B-mode behind the free wall of the right ventricle. EFT was considered as an increase EFT≥7 mm, which showed association with cardiometabolic disorders in clinical studies. Group 1 included 50 patients with a metabolic healthy obesity phenotype (MHO) who had EFT <7 mm and I degree of general obesity (BMI 30-34,9 g/m2). In Group 2, 60 patients with metabolic fat obesity phenotype (MFO) (EFT ≥7 mm) and without general obesity (BMI <30 kg /m2). All subjects underwent lipid spectrum estimation, adipokines level measurements: leptin, adiponectin, insulin metabolism parameters were also determined: insulin level, insulin resistance index HOMA-IR. All patients were also evaluated according to abdominal obesity (AO) in terms of waist circumference (WC).

Results. Analyzing the level of adipokines in the group of MFO (EFT≥7 mm) it is obvious that the leptin level was significantly higher, and the level of cardioprotective adiponectin was significantly lower than in MHO group (EFT <7 mm) (32.16 ± 5.46 ng / ml vs. 14.92 ± 3 , 30 ng / ml, p = 0.001, 15.14 ± 3.78 μg / ml versus 27.41 ± 2.42 μg / ml, p = 0.01, respectively). The low density lipoprotein cholesterol (LDL-C) cholesterol levels in the MFO group were significantly higher, and the high density lipoprotein cholesterol (HDL-C) values were lower than the MHO group (3.73 ± 0.82 mmol / L vs. 3.13 ± 1.17 mmol / L, p = 0.001, 1.02 ± 0.22 mmol / L versus 1.26 ± 0.44 mmol / l, p = 0.03). Assessing insulin metabolism in group 2, higher values of insulin and HOMA-IR index were observed than the ones in group 1 (9.37 ± 2.07 μIU / ml vs. 5.97 ± 0.97 μIU / ml, p = 0.001; 2,16 ± 0,50 against 1,35 ± 0,29, p = 0,001, respectively). As a result of the analysis of the datum, it was revealed that in the MFO group, 11 patients had IR (HOMA-IR≥2.77). With the help of linear regression analysis, the threshold value of EFT was determined, from which the IR with HOMA-IR≥2.77 began to be determined. This figure was 9.5 mm. In the study groups, there were no statistical differences in the WC (95.68 ± 3.32 cm in group 1 versus 97.52 ± 3.78 cm in group 2, p = 0.053). In assessing the relationship among different obesity indicators: WC, BMI, EFT (as an indicator of epicardial obesity (EO)) with major and additional metabolic risk factores in groups with different MFO, a significant positive correlation was found among the EFT and insulin, the HOMA-IR index, TG, LDL-C in the MFO group (R = 0.78, p = 0.001; r = 0.8; p = 0.001; r = 0.61; p = 0.001; r = 0.6; p = 0.001, respectively). WC significantly correlated only with BMI in both the MFO group and the MHO group (r = 0.65, p = 0.01, r = 0.73, p = 0.001, respectively), with other metabolic risk factors of the correlation relationship of WC, as well as BMI, was not found.

Conclusions. EO has a significant impact on the formation of the MFO. EFT may be a significant predictor of cardiometabolic risk. The low prognostic significance of WC and BMI for cardiovascular risk has been established.

THE EFFECT OF LEPTIN RESISTANCE ON THE FORMATION OF A METABOLICALLY FAT OBESITY PHENOTYPE

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For the evaluation of cardiovascular risk (CVR), it is proposed to isolate various metabolic phenotypes of obesity: the metabolic fat phenotype of obesity (MFO) with the predominance of visceral fat (VF) over the subcutaneous and the presence of cardiometabolic disorders and the metabolic healthy obesity phenotype (MHO), in which there is subcutaneous obesity, there is no visceral obesity (VO), and a normal cardiometabolic profile is maintained. The role of leptin resistance (LR) in the formation of MFO is actively studied. At the heart of LR, leading to hyperleptinemia, insulin resistance (IR), VO, CVR, is a violation of receptor sensitivity to leptin in the hypothalamus or a decrease in the amount of soluble receptors for leptin (SLR). According to a few literature data, it is proposed to use the free leptin index (FLI) calculated as the ratio of serum leptin (SL) to the level of SLR, which showed the relationship with CVR and IR. The purpose of the study: To study the influence of FLI, as a laboratory marker of the LR, on the formation of the MFO. Materials and methods. The study included 110 men, 52.3 ± 3.5 years old, with arterial hypertension (AH) and the absence of clinical manifestations of atherosclerosis of any localization, type 2 diabetes. Two groups were formed, according to the metabolic phenotypes of obesity for epicardial fat thickness (EFT) (as a type of VO) and body mass index (BMI). Estimation of EFT was carried out by echocardiography in B-mode behind the free wall of the right ventricle. Epicardial obesity (EO) was considered to be an increase in EFT≥7 mm, which in clinical studies showed an association with cardiometabolic disorders. Group 1 included 50 patients with a metabolic healthy obesity phenotype (MHO) who had EFT <7 mm and I degree of general obesity (BMI 30-34,9 kg/m2) . In Group 2 there were 60 patients with a metabolic fat obesity phenotype (MFO) (EFT≥7 mm) and without general obesity (BMI <30 kg / m2). All the subjects underwent lipid and leptin metabolism evaluation: SL, SLR, FLI, insulin exchange: insulin levels, insulin resistance index HOMA-IR.

Results. Assessing lipid metabolism in the MFO group, the low density lipoprotein cholesterol (LDL-C) levels, triglycerides(TG), and Apo B proteins in the MFO group were significantly higher, and the high density lipoprotein cholesterol (HDL-C) and Apo A proteins levels were significantly lower than the MHO group (3 , 73 ± 0.82 mmol/l vs. 3.13 ± 1.17 mmol / l, p = 0.001, 2.09 ± 0.48 mmol / L vs. 1.70 ± 0.43 mmol / l, p = 0.003, 1, 06 ± 0,14 g / l against 0,85 ± 0,07 g / l, p = 0,0001, 1,02 ± 0,22 mmol / l against 1,26 ± 0,44 mmol / l, p = 0.03, 0.84 ± 0.13 g / l versus 1.27 ± 0.38 g / l, p = 0.0001, respectively). Analyzing the parameters of LR in the group of MFO (EFT≥7 mm), the levels of leptin and FLI were significantly higher, and the SLR levels were significantly lower than the MHO group (EFT <7 mm) (32.16 ± 5.46 ng / ml vs. 14.92 ± 3.30 ng / ml, 1.67 ± 0.58 vs. 0.37 ± 0.09, 20.80 ± 5.22 ng / ml vs 41.64 ± 5.91 ng / ml, p = 0.001, respectively). In the correlation analysis among FLI and risk factors in the MFO group, a significant positive correlation of FLI with EFT, insulin, HOMA-IR index was found, with the greatest interrelation force between FLI and HOMA-IR (r = 0.38; r = 0.35, r = 0.67, p = 0.001, respectively). Using a linear regression analysis, a threshold value of the FLI of 1.52 was obtained, from which the EO with a EFT≥ 7 mm began to be determined. Assessing insulin metabolism in the MFO group, higher values of insulin and HOMA-IR index were observed than in the group of MHO (9.37 ± 2.07 μIU / ml vs. 5.97 ± 0.97 μIU / ml, p = 0.001; 2.16 ± 0.50 against 1.35 ± 0.29, p = 0.001, respectively). In the MFO group, 11 patients had IR (HOMA-IR≥2.77). FLI in the subgroup of IR was significantly higher than the subgroup without IR (2.15 ± 0.68 vs. 1.56 ± 0.5, p = 0.005). Using a linear regression analysis, a threshold value of the FLI of 1.87 was determined, from which the determination of the IR with HOMA-IR ≥ 2.77 started.

Conclusions. Leptin resistance (LR) has a significant effect on the formation of the MFO. According to the significant correlation between the FLI and the HOMA-IR index in the MFO group (r = 0.67, p = 0.001), we propose to use the FLI of 1.87 as the LR criterion.

THE C(-915)G POLYMORPHISM OF TRANSFORMING GROWTH FACTOR BETA-1 GENE AND RISK OF ATRIAL FIBRILLATION IN PATIENTS WITH METABOLIC SYNDROME

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Introduction. Metabolic syndrome (MetS) increases the risk of atrial fibrillation (AF). Transforming growth factor β1 (TGF-β1) – an inductor of myocardial fibrosis specially in the atria.

Aim. To study the distribution of CC, CG and GG genotypes C(-915)G polymorphism of TGF-β1 gene in patients with MetS with AF.

Materials and methods. In a study were included 424 people (156 male and 268 female) with a mean age of 47,8 ± 11,0 years: 198 patients with MetS, including 103 patients with paroxysmal and permanent AF. The control group included 226 healthy humans without cardiovascular disease and metabolic disorders. Genomic DNA was isolated from whole venous blood. Allelic variants identified by PCR followed by restriction analysis with endonuclease BglI.

Results. Carriage of GG genotype C(-915)G TGF-β1 gene in patients with MetS and AF occurred more frequently than in MetS patients without AF (97,1% and 86,3%, p=0,012) and more frequently than in healthy (97,1% and 87,2%, p=0,009). Carriage of GG genotype increased the risk of AF in patients with MetS (OR = 5,28, 95%CI 1,46-19,18, p=0,012). The differences in carriage of GG genotype C(-915)G TGF-β1 gene in MetS patients without AF and healthy were not found (p = 0.836).

Carriage of G allele in the group MetS with AF occurred more frequently than in patients with MetS without AF (98,5% and 93,2%, p = 0,014) and more frequently than in healthy control (98,5% and 93,1%, p = 0,007). Carriage of G allele gene TGF-β1 increased the risk of AF in patients with MetS (OR = 4,97, 95%CI 1,39-17,72, p = 0,014). The differences in carriage of G allele in patients with MetS without AF and healthy were not found (p = 0,994).

Conclusions. In the study established association of GG genotype C(-915)G and G allele of the TGF-β1 gene with the probability of atrial fibrillation in patients with metabolic syndrome. We propose that increased expression of genes TGF-β1 causes heterogeneity of conduction and contributes to atrial fibrillation in patients with metabolic syndrome.

ALTERATIONS IN CARDIAC ENERGY METABOLISM IN HEART FAILURE DUE TO DILATED CARDIOMYOPATHY: THE ROLE OF PEROXISOME PROLIFERATOR ACTIVATED RECEPTORS

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Dilated cardiomyopathy (DCM) is one of the main causes of heart failure (HF). Myocardial metabolism is altered in heart failure, and heart failure itself is associated with significant metabolic abnormalities, failing hearts become energy deprived. The nuclear receptor peroxisome proliferator activated receptor-alpha (PPAR alpha) and PPAR-gamma coactivator-1alpha (PGC-1 alpha) play important roles in regulation of myocardial metabolism and contribute significantly to the changes that occur in the failing heart. PPAR alpha and PGC-1 alpha control homeostasis of fatty acids – the main source of energy in a healthy heart through transcriptional activation of genes encoding

the key proteins of fatty acid metabolism, that regulate uptake and oxidation of fatty acids. In animal models of heart failure accumulation of lipids within cardiomyocytes is associated with contractile dysfunction. Patients with HF and diabetes and/or obesity exhibited significant intramyocardial lipid deposition and upregulation of PPAR alpha and PGC-1 alpha. The accumulation of excess lipid within cardiomyocytes may lead to the production of toxic lipid intermediates, which can induce cell death. Such cardiac lipotoxicity refers to the constellation of altered fatty acid metabolism, intramyocardial lipid overload, and contractile dysfunction. However, whether intramyocardial lipid deposition is a feature of human HF due to DCM remains to be established.

The aim of this study was to examine gene expression levels of PPAR alpha, PGC-1 alpha and PPARα target genes and intramyocardial lipid accumulation in patients with HF due to DCM.

Material and methods: Endomyocardial biopsies were obtained from patients with dilated cardiomyopathy and heart failure. Oil red O staining was performed on heart sections. Quantitative RT-PCR was used to measure PPARα – a key regulator of fatty acid β-oxidation, PGC-1 alpha and PPARα target genes: Long-Chain Acyl-CoA Dehydrogenase (LCAD, a key enzyme of β-oxidation); Cardiac Carnitine Palmitoyl-Transferase-1 (CPT-1, the other principal outer mitochondrial membrane fatty acid transporter); Cluster-of-Differentiation 36 (CD36, also known as Fatty-Acid Translocase (FAT); Heart Fatty-Acid-Binding Protein (HFABP) gene expression levels in the same samples.

Results: In our study 30 endomyocardial biopsies from patients with dilated cardiomyopathy and heart failure were analyzed. All samples demonstrated low oil red O staining. The results have shown significant decreased PPAR alpha and PGC-1 alpha gene expression levels in failing hearts compared with nonfailing hearts. Transcript expression levels of CD36, CPT-1 and LCAD decreased in DCM in comparison to human non-diseased myocardium autopsy specimens. The significant up-regulation of HFABP was observed in the study.

Conclusion: The downregulation of PPAR alpha and PGC-1 alpha demonstrates the changes in cardiac energy metabolism, characterized by the shift from fatty acid oxidation to glucose oxidation as the main energy source. As the results have shown low intramyocardial lipid accumulation in the samples, therefore the alterations in fatty acid metabolism in dilated cardiomyopathy and heart failure do not lead to accumulation of intramyocardial lipids and cardiac lipotoxicity. Downregulation of PPAR alpha and PGC-1 alpha results to the deactivation of genes encoding key proteins of fatty acid metabolism, including genes involved in fatty acid delivery into cardiomyocytes. Consequently contractile dysfunction in dilated cardiomyopathy and heart failure is not associated with accumulation of lipids within cardiomyocytes. It can be assumed that the regulation of the cardiac energy metabolism is possible by acting on PPARα, PGC-1 alpha, CD36, CPT-1, LCAD and HFABP.

CHOICE OF THE REVASCULARIZATION METHOD IN PATIENTS WITH PEREFIRIAL ATHEROSCLEROSIS ON THE BACKGROUND OF METABOLIC SYNDROME

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Metabolic syndrome (MS) and its components are factors that determine outcomes of reconstructive interventions in case of peripheral arterial disease (PAD).

The aim of the research is to identify associations between the presence of MS and the choice of a reconstruction option in patients with PAD.

Materials and Methods: The work is based on observation of 73 patients with PAD on the background of MS, who underwent revascularization (mainly about critical ischemia (CLI)). The main group consists of 48 patients who

underwent endovascular interventions (EI), mainly in the infrainguinal segment. The control group consists of 25 patients who underwent traditional (open) operations (OO). We analyzed: the duration of hospitalization, the duration of the operation, the blood loss volume, the dynamics of tissue oxygenation (as a result of the intervention), complications, and the preservation of the limb within 30 days after the intervention. MS was diagnosed by the ATP III criteria.

Statistical processing was performed using "STATISTICA-10" software package. The value "p <0.05" is indicated as statistically significant.

Results: There are a lot of patients with MS with high perioperative risk and severe comorbid conditions (stage 2-3 hypertension, diabetes, etc.). At the same time, we can perform revascularization (including patients with CLI background) through EV taking into account the characteristics of atherosclerotic lesions according to TASC II. The gender characteristics of PAD determine the predominance of women in the endovasal group. Tolerability of EV is associated with minimal blood loss and insignificant duration of these effects in comparison with OO in MS patients (85 ± 49 min v / s 211 ± 103 min, p <0.05). Low invasiveness of EV, however, is characterized by an adequate clinical effect (pO2 level in tissues in this group had better dynamics than in the OO group). The greater number of complications in the OO group is accompanied by an increase in the duration of the bed-day compared with the EV group (p <0.05).

CAUSES OF HYPERFUSION SYNDROME AFTER CAROTID ENDARTERECTOMY

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Hyperperfusion syndrome (HS) – is a common negative consequence of carotid endarterectomy.

The aim of the research is to reveal the predictors of the development of the HS after performing carotid endarterectomy (CEA).

Materials and Methods: The study is based on the observation of 83 patients who underwent CEA, among whom 23 patients had asymptomatic carotid stenosis, 60 patients had neurological symptoms. The main group consists of 20 patients with HS after CEA, the control group – 63 patients who did not have any HS manifestations. We analyzed: the severity of metabolic disorders in operated patients, changes in cognitive functions according to the MoCA scale, peculiarities of the perioperative period, deviations in arterial pressure, peculiarities of comorbid conditions and consequences of surgical intervention.

Statistical processing was performed using "STATISTICA-10" software package. The value "p <0.05" is indicated as statistically significant.

Results: Patients with HS had a history of transient ischemic attacks (TIA) more frequently than patients in the control group (6 v / s 2, p <0.05). In patients with HS, the manifestations of dyslipidemia were more common: the level of total cholesterol in the main group was 7.0 ± 1.2 mmol / l, the LDL level was 3.6 ± 0.6 mmol / l, in the control group – 4, 9 ± 1.2 mmol / L and 2.9 ± 0.7 mmol / L, respectively (p <0.05). In the main group, signs of carbohydrate disturbances were more often than in the control group (blood glucose level was 7.0 ± 1.5 v / s 5.6 ± 0.6, respectively, p <0.05).

Stenosis of the contralateral carotid artery was noted more frequently in patients with signs of HS in the postoperative period (87 ± 5.9% v / s 69.5 ± 16.8%, respectively, p <0.05). Hemodynamically significant lesions of the vertebral and subclavian arteries were also more common among patients with HS when compared with the patients without such complications (25% and 95% v / s 1.59% and 20.63%, respectively, p <0.05).

Conclusions: Correction of metabolic disorders and monitoring of perioperative hemodynamics is the basis of HS prevention.

FATTY LIVER DISEASE: ULTRASOUND STUDY IN SIBERIAN POPULATION

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Fatty liver disease (FLD) is associated with insulin resistance, metabolic syndrome and might be related to excess alcohol consumption. Non-alcohol fatty liver disease (NAFLD) and alcohol fatty liver disease (AFLD) have common components of pathogenesis. Nowadays FLD is considered as a predictor of cardiovascular risk. There are little knowledge about prevalence and mechanisms of FLD in Russia which is characterized by high cardiovascular mortality and diverse patterns of alcohol intake.

Purpose: To investigate the prevalence of FLD by ultrasound study (US) and analyze risk factors, associated with sonographic pattern of steatosis in men and women in Siberian population.

Methods: The study was founded on the data of the WHO MONICA Project in Novosibirsk. A random population sub-sample included 1155 men and 870 women in aged 25-64 years. FLD was identified by US established criteria. The association of FLD with potential determinants was estimated in logistic regression.

Results: The prevalence of FLD was 20% in men and 19% in women. In men, its multivariable-adjusted predictors included: age, body mass index (BMI), level of triglycerides and frequency of alcohol intake or high occasional dose (≥120g of ethanol) - odds ratio [OR] 2.6, p=0.002 for ≥120g of ethanol per typical drinking session and frequent drinking [OR] 9.2, p<0.001, for drinking more than once a week compared with non-drinkers. In women, in age-adjusted model we have revealed the association between FLD and BMI, level of total cholesterol, HDL-cholesterol and triglycerides, and diabetes mellitus. In multivariable-adjusted model the association between FLD and BMI remained significant only-[OR] 14.8, p<0.001, for BMI ≥35 vs. <25) and has not association with any alcohol measure.

Conclusions: The prevalence of FLD by sonography was equaled about 20% for men and women. These data are comparable with data from European, North American and Asian populations. FLD and its determinants have gender differences: for women the most characteristic having NAFLD (13%); men have NAFLD and AFLD in equal parts (6.2 %). In men, FLD was attributable by the age, metabolic indicators, frequency of alcohol intake and high doses of ethanol per session (≥120g); in women, FLD are independently associated to high BMI.

THE EXPRESSION OF THE LEPTIN, DOPAMINE AND SEROTONIN RECEPTORS IN HYPOTHALAMIC POMC-NEURONS IN NORM AND OBESITY

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In the hypothalamus, the leptin and monoaminergic systems are involved in regulation of activity of melanocortin signaling system, controlling the expression of anorexigenic and orexigenic peptides. It is assumed that these systems can participate in the control of expression of pro-opiomelanocortin (POMC), a precursor of anorexigenic melanocortin peptides that is produced by POMC/CART-neurons of the arcuate nucleus (ARC) of hypothalamus. The POMC-derived melanocortin peptides have a key role in regulation of food intake and energy expenditure and are responsible for insulin sensitivity and lipid metabolism in the periphery. However, the data on the interrelation between the hypothalamic dopamine and serotonin systems and the production of

POMC in the ARC are few or absent. The aim of this work was to study the expression and localization of types 1 and 2 dopamine receptors (D_1- and D_2-DR), types 1B and 2C serotonin receptors (5-HT_{1B}R and 5-HT_{2C}R) and leptin receptors (LepR) on POMC-neurons of the ARC in normal and obese rodents. In the experiments, normal C57Bl/6J mice and obese agouti mice, as well as control Wistar rats and the rats with obesity induced by high fat/high carbohydrate diet were used. The D_1- and D_2-DR were located on POMC-neurons in both rodent species, and the expression of D_2-DR in POMC-neurons was higher than D_1-DR, which indicates a close relationship between D_2-DR and POMC production. In the ARC of obese rodents the expression of both types of DR was reduced. The 5-HT_{1B}R and 5-HT_{2C}R was also intensively expressed in POMC-neurons, and the expression of 5-HT_{2C}R was more pronounced. In obesity the number of 5-HT_{1B}R and 5-HT_{2C}R in POMC-neurons did not change significantly, but the alterations in their localization were detected. The expression of LepR in the POMC-neurons of obese rats was increased, but in agouti mice the expression of the same receptor did not change significantly as compared to C57Bl/6J mice. The obtained data speaks in favor that the dopamine and serotonin signaling systems can be involved in the functioning of POMC-neurons and mediate monoamine-induced regulation of feeding behavior and energy homeostasis. In obesity the activity of these systems was changed, which contributes to the development of obesity and other metabolic disorders.

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