International Heart and Vascular Disease Journal
Volume 2, Number 4, November 2014

Journal of the Cardioprogress Foundation

Review of international clinical trials in cardiology reported in 2014

Oganov R.G., Kanorskiy S.G., Mamedov M.N.*

State Budget Educational Institution of Higher Professional Education "Kuban State Medical University" of the Ministry of Healthcare of the Russian Federation, 350063, Russia, Krasnodar, 4 Sedin Street

Authors:

Rafael G. Oganov, MD, Professor, Academician of Russian Academy of Medical Sciences, Head of the Department for Prevention of Comorbid Conditions, National Research Centre for Preventive Medicine of the Ministry of Healthcare of the Russian Federation, Moscow, Russia

Sergey G. Kanorskiy, MD, Professor, Head of the Department of Therapy №2 of Faculty of Advanced Training and Professional Retraining of Specialists of the State Budget Educational Institution of Higher Professional Education "Kuban State Medical University" of the Ministry of Healthcare of the Russian Federation, Krasnodar, Russia

Mehman N. Mamedov, MD, Professor, Head of the Laboratory for Interdisciplinary Approaches on the Prevention of Chronic Non-communicable Diseases, National Research Centre for Preventive Medicine of the Ministry of Healthcare of the Russian Federation, Moscow, Russia

Summary

In this review article we summarized the results of 28 large international clinical studies presented in the framework of five scientific Hot Line sessions at the European Society of Cardiology Congress 2014. The analyzed studies cover a wide range of issues on diagnosis, treatment and prevention of cardiovascular disease (CVD).

Keywords

Cardiovascular disease, clinical studies

* Corresponding author. Tel. +7 926 228 33 09. Fax. +7 499 5536 903. Email: mmamedov@mail.ru.

Every year at the scientific Hot Line sessions of the European Society of Cardiology Congress, results of large completed clinical studies are traditionally presented. The last European Congress which was held between 30 August and 03 September 2014 in Barcelona (Spain) was no exception. To conduct a review analysis, the results of 28 international clinical trials within five scientific Hot Line sessions were used. In general, the presented studies cover a wide range of issues on diagnosis, treatment and prevention of CVD.

Clinical studies presented at the scientific Hot Line I session – Cardiovascular disease: novel therapies

Angiotensin-converting enzyme (ACE) inhibitors have been the primary means of treatment of chronic heart failure (CHF) patients with reduced left ventricular ejection fraction (LVEF) for almost 3 decades, and enalapril was proved to reduce the risk of death in these patients. Neprilysin is a neutral endopeptidase, degrading endogenous vasoactive substances: natriuretic peptides, bradykinin and adrenomedullin. Neprilysin inhibition increases the levels of these substances, which prevents excessive neurohormonal activation, responsible for vasoconstriction, sodium retention and maladaptive remodeling. In the PARADIGM-HF (Efficacy and Safety of LCZ696 Compared to Enalapril on Morbidity and Mortality in Patients with Chronic Heart Failure) study [1], patients with any classes of CHF, usually New York Heart Association (NYHA) functional class II/III, and LVEF ⩽40%, which were, in the background of the recommended therapy, randomized for an additional intake of an experimental drug LCZ696 (a combination of valsartan and sacubitril (neprilysin inhibitor)) – 200 mg 2 times a day (n=4.187) or enalapril – 10 mg 2 times a day (n=4.212). The study was stopped prematurely at 27 month mean follow-up of patients due to the apparent benefits of LCZ696. The primary endpoint (cardiovascular death or hospitalization because of CHF) was recorded 20% (P<0.0000002) less often, death from cardiovascular cause – 20% (P=0.00004), hospitalization due to CHF – 21% (P<0.001), and death from any cause – 16% (P<0.001) less often, respectively, in the group of LCZ696 therapy. Treatment with LCZ696, compared to enalapril, has been often accompanied by hypotension and mild angiooedema, less often – by renal failure, hyperkalaemia, and cough. Superiority of LCZ696 over enalapril in reducing the risk of death and hospitalization due to CHF suggests that a new drug can replace ACE inhibitors and angiotensin II receptor blockers in the treatment of CHF.

It is assumed that under the conditions of sympathetic hyperactivity typical for CHF, an increase of vagal influences on the heart is able to align the neurohumoral imbalance and slow down the progression of the disease. In the first randomized NECTAR-HF (NEural Cardiac TherApy foR Heart Failure) trial [2], assessing this idea, 96 patients with symptomatic CHF were involved. The patients underwent electrical stimulation of the right vagus nerve in the neck (the mean pulse amplitude of 1.24 mA first and 1.42 mA after 3 months, frequency of 20 Hz) or were performed a simulation of stimulation. After 6 months the decrease in left ventricular (LV) end-systolic diameter (the primary endpoint) was 0.04±0.25 cm in the therapy group and 0.08±0.32 cm in the control group (P=0.60). Other echocardiographic parameters, maximal oxygen consumption during exercise, and the level of N-terminal brain natriuretic peptide precursor also did not differ in groups of real and imaginary vagus nerve stimulation. There was a statistically significant improvement in quality of life according to the Minnesota Living with Heart Failure Questionnaire (MLHFQ) (P=0.049) and the physical component according to the 36-item Short Form (SF-36) Health Survey (P=0.016) and NYHA Functional Classification (FC) (P=0.032) in the therapy group. Surprisingly often (7.4% of cases), infectious complications occurred. As a result, it was failed to demonstrate a significant effect of right-sided vagus nerve stimulation on heart remodeling and exercise tolerance in patients with symptomatic CHF.

Iron deficiency occurs in about half of patients with CHF, which leads to deterioration of their functional status, quality of life and increased mortality. The CONFIRM-HF (Ferric CarboxymaltOse evaluatioN on perFormance in patients with IRon deficiency in coMbination with chronic Heart Failure) study [3] included 304 patients with symptomatic CHF and LVEF⩽45%, increased levels of natriuretic peptide and iron deficiency (ferritin <100 ng/mL or 100–300 ng/mL, if transferrin saturation <20%). After randomization, in addition to the recommended treatment of CHF in half of the cases, intravenous ferric carboxymaltose was re-applied, and the other half received placebo, monitoring the results of the treatment during 52 weeks. Ferric carboxymaltose significantly (33±11 metres; P=0.002) prolonged the distance of 6-minute walk after 24 weeks (primary endpoint) compared with placebo, improved NYHA FC of CHF, quality of life, reduced symptoms, and lowered the risk of CHF hospitalization by 61% (P=0.009). The frequency of adverse events in the groups did not differ significantly.

Intravenous administration of iron supplement is not yet recommended for the treatment of CHF, but very useful when identifying iron deficiency.

During cardiac resynchronization therapy (CRT) with LV stimulation by bipolar electrode, it is often not possible to achieve simultaneous contraction of the ventricles. The MORE-CRT (More Options available with a quadripolar LV lead pRovidE in-clinic solutions to CRT challenges) [4] study compared the quadrupole electrical stimulation of LV by Quarter™ (n=720) with traditional bipolar (n=348). Survival without intra- and postoperative complications within 6 months (primary endpoint) was observed in 85.97% and 76.86% of cases using the quadrupole and bipolar electrodes, respectively (P=0.0001) – relative risk reduction by 40.8%. Intraoperative complications occurred in 5.98% vs. 13.73% of cases (P<0.0001) in groups of the quadrupole and bipolar electrical stimulation of LV, respectively.

After heart surgery, pericardial effusion is found in 50-85% of patients, and 1–2% develop pericardial tamponade. In the randomized POPE-2 (Post-Operative Pericardial Effusion-2) [5] trial in patients underwent coronary artery bypass surgery, heart valve or aortic surgeries, 1 mg/day of colchicine (n=98) or placebo (n=99) were used for 14 days, estimating the frequency of pericardial effusion (primary endpoint) for 30 days. Colchicine, comparable to the placebo, influenced the severity of the pleural effusion according to echocardiography (P=0.23), frequency of pericardial tamponade (P=0.80), and the need to drain its cavity, in other words, did not provide with the desired therapeutic effect.

Postpericardiotomy syndrome and postoperative atrial fibrillation (AF) worsen morbidity and increase the costs of treating patients who underwent coronary artery bypass surgery or surgery on the heart valves. Such patients with sinus rhythm in the COPPS-2 (COlchicine for Prevention of the Post-pericardiotomy Syndrome and Post-operative Atrial Fibrillation) trial [6] were appointed after randomization colchicine (n=180) 0.5 mg 2 times a day or 0.5 mg once a day if body weight <70 kg 48–72 hours prior to surgery and for 1 month thereafter or placebo (n=180). Postpericardiotomy syndrom (primary endpoint) was detected in 19.4% of patients treated with colchicine and in 29.4% – placebo. However, the incidence of postoperative AF and significant pericardial effusion in two groups were not significantly different. Observed side effects of colchicine from the gastrointestinal tract limit its potential advantages when used in cardiac surgery.

Clinical studies presented at the scientific Hot Line II session – Coronary artery disease and lipids

Lipoprotein-associated phospholipase A2 is an enzyme that is secreted by leukocytes and binds to circulating lipoproteins and macrophages of atherosclerotic plaques. It is considered as a marker of inflammation of the arteries, predictor of plague destabilization and vascular complications. The SOLID-TIMI 52 (Stabilization Of pLaques usIng Darapladib-Thrombolysis In Myocardial Infarction 52) study [7] of a direct inhibitor of this enzyme, darapladib, included patients hospitalized for acute coronary syndrome in the last 30 days. After randomization, in addition to recommended therapy patients were assigned darapladib (n=6,504) or placebo (n=6,522). After an average of 2.5 years of treatment, darapladib did not reduce, compared with placebo, total number of deaths from coronary artery disease (CAD), myocardial infarction (MI), and emergency coronary revascularization for myocardial ischaemia (primary endpoint) (P=0.93), cardiovascular death, MI, or stroke (P=0.78), and total mortality (P=0.40).

Increased heart rate (HR) is a recognized marker of the risk of cardiovascular complications. It was previously shown that ivabradine improves outcomes in patients with stable CAD, LV dysfunction and sinus rate ≥70 beats per minute (bpm). The SIGNIFY (Study assessInG the morbidity–mortality beNefits of the If inhibitor ivabradine in patients with coronarY artery disease) study [8] included patients with stable CAD without CHF and with sinus rhythm ≥70 bpm, in most cases with FC ≥II activity-limiting angina. After randomization, ivabradine was added to the recommended therapy at a dose of 10 mg 2 times a day (n=9,550) (the target heart rate from 55 to 60 bpm) or placebo (n=9,552). After 3 months an average sinus rhythm was 60.7±9.0 bpm in a group of ivabradine vs. 70.6±10.1 bpm in the placebo group. At an average of 27.8-month follow-up, death from cardiovascular causes or non-fatal MI (primary endpoint) was detected in 6.8% and 6.4% of cases (P=0.20) in the ivabradine and placebo groups, respectively, with no significant differences in the incidence of death from cardiovascular causes and non-fatal MI. Ivabradine intake was associated with an increase in the frequency of the primary endpoint in patients with activity-limiting angina, but not in patients without such angina. Bradycardia was observed in 18.0% and 2.3% of patients (P<0.001) in the ivabradine and placebo groups, respectively. It is likely that in patients with stable CAD and normal LVEF, increased heart rate is

a marker of risk, but not modifiable determinant of outcomes.

Proprotein convertase subtilisin/kexin type 9 is a molecule that plays a key role in the destruction of low-density lipoprotein (LDL) receptors, which leads to a decrease in the capture and catabolism of circulating LDL, and an increase in their plasma levels. Alirocumab is a fully human monoclonal antibody of above molecule, effectively correcting hypercholesterolaemia. The ODYSSEY COMBO II (Efficacy and Safety of Alirocumab Versus Ezetimibe on Top of Statin in High Cardiovascular Risk Patients with Hypercholesterolemia) study [9] included patients with history of CVD and LDL ≥1.8 mmol/L or with risk factors and LDL ≥2.6 mmol/L despite treatment with the maximum tolerated daily dose of statin. After randomization, there was further application of alirocumab 75 mg (18.4% of cases – 150 mg) subcutaneously every 2 weeks (n=479) or ezetimibe 10 mg/day (n=241). After 24 weeks, a reduction in LDL was noted by 50.6% and 20.7% (*P*=0.0001), with the achievement of its levels <1.8 mmol/L in 77% and 45% of cases in groups of alirocumab and ezetimibe, respectively. The frequency of alirocumab or ezetimibe discontinuation due to the side-effects (most often, vertigo and myalgia) was 7.5% and 5.4%, respectively.

The ODYSSEY FH I (Efficacy and Safety of Alirocumab Versus Placebo on Top of Lipid-Modifying Therapy in Patients With Heterozygous Familial Hypercholesterolemia Not Adequately Controlled With Their Lipid-Modifying Therapy) [10] and FH II (Study of Alirocumab in Patients With Heterozygous Familial Hypercholesterolemia Who Are Not Adequately Controlled With Their Lipid-Modifying Therapy) [11] studies included patients with two genetic variants of heterozygous familial hypercholesterolaemia and insufficient effect of the maximum tolerated daily dose of statin or other therapy. After randomization, alirocumab 75 mg subcutaneously every 2 weeks increasing its dose to 150 mg if after 8 weeks LDL remained ≥1.8 mmol/L or placebo were added to the treatment. After 24 weeks at the first genetic variant of hypercholesterolaemia, alirocumab (n=323) reduced LDL by 48.8%, placebo (n=163) – by 9.1% (*P* < 0.0001), while at the second variant of hypercholesterolaemia, alirocumab (n=167) reduced LDL by 48.7%, placebo (n=82) – by 2.8% (*P*<0.0001). As a result, the target LDL levels were achieved in >70% of patients and >80% of patients with two investigated variants of heterozygous familial hypercholesterolaemia with the cancellation frequency of alirocumaba because of side effects (injection site reactions, nasopharyngitis, headache) in 3.1% and 3.7% of cases, respectively.

The ODYSSEY Long Term (Long-term Safety and Tolerability of Alirocumab Versus Placebo on Top of Lipid-Modifying Therapy in High Cardiovascular Risk Patients With Hypercholesterolemia) study [12] included patients with CAD, high risk of cardiovascular complications or heterozygous familial hypercholesterolaemia (17.7% of cases) and LDL levels ≥1.81 mmol/L in the background of receiving the maximum tolerated dose of statins and/or other lipid-lowering therapy. After 24 weeks of alirocumab application (n=1,553) in dose of 150 mg subcutaneously every 2 weeks or placebo (n=788), LDL levels decreased by 61.0% and 0.8%, respectively (*P* < 0.0001), reaching on average 1.25 mmol/L vs. 3.08 mmol/L. There was retrospectively found a decrease in total incidence of coronary death, non-fatal MI, fatal and non-fatal ischemic stroke, and unstable angina requiring hospitalization by 54% (*P*=0.0089). The incidence of discontinuation in alirocumab and placebo groups was 6.2% and 5.5%, respectively.

Statins can increase the risk of diabetes, but their influence on the course of existing diabetes has not been sufficiently studied. In the LISTEN (LIpid lowering with highly potent Statins in hyperlipidemia with Type 2 diabetes patiENts) study [13], Japanese patients with type 2 diabetes and hypercholesterolaemia were given after randomization rosuvastatin 5 mg/day (n=514) or atorvastatin 10 mg/day (n=504) during one year. After 3 months, LDL levels decreased in groups of rosuvastatin and atorvastatin by 39.4% and 36.4% (*P*=0.0106), and after a year – by 34.8% and 32.8%, respectively. Blood glucose levels after 3 and 6 months increased more under effect of atorvastatin (*P*=0.0104), but in a year, they changed equally, on average by 0.11% and 0.12%, in groups of rosuvastatin and atorvastatin, respectively. At the same time, 1.46 times greater (*P*=0.05) number of patients treated with atorvastatin, received enhanced diabetes therapy to correct the observed hyperglycaemia. Therefore, rosuvastatin is the best treatment choice for patients with type 2 diabetes compared with atorvastatin.

Clinical studies presented at the scientific Hot Line III session – Heart failure: devices and interventions

Improvement of a stent design, affecting the thickness of their wall, surface of the polymer and a drug release, resulted in the improvement of clinical outcomes by using drug-eluting stents. In the BIOSCIENCE (Ultrathin strut biodegradable poly-

mer sirolimus-eluting stent versus durable polymer everolimus-eluting stent for percutaneous coronary revascularisation) study [14], patients with stable CAD or acute coronary syndromes had compared the efficacy and safety of a new ultrafine cobalt chromium stent releasing sirolimus from a biodegradable polymer, and thin stent releasing everolimus from a durable polymer. In 1,063 patients treated with sirolimus-eluting and 1,056 with everolimus-eluting stents, cumulative incidence of complications (cardiac death, MI in the area of the target artery, revascularization – primary endpoint) during 12 months was 6.5% and 6.6% (P=0.0004 for noninferiority), the frequency of stent thrombosis was 0.9% and 0.4% of cases (P=0.16), respectively. A decrease of primary endpoint events was reported in patients with biodegradable stents in the subgroup of patients with ST segment elevation MI (STEMI) (3.3% vs. 8.7%; P=0.024), which requires further study.

Vegetative regulating therapy by stimulating the vagus nerve on the right (n=29) or left (n=31) of the neck area was evaluated in the ANTHEM-HF (Autonomic Neural Regulation Therapy to Enhance Myocardial Function in Heart Failure) study [15] in patients with NYHA FC II / III CHF and LVEF ⩽40%, receiving optimal pharmacotherapy. Electrical stimulation was performed by current pulses of 2.0±0.6 mA with a natural frequency (10 Hz) and was well tolerated regardless of the stimulation side, and it rarely caused mild dysphonia, cough or pain in the oropharynx. After 6 months of vegetative regulating therapy, LVEF increased on average by 4.5%, LV end-systolic volume decreased by 4.1 mL, NYHA FC was improved in 77% of patients, and the six minute walking distance was lengthened by 56 and 77 m at the left and right electrical stimulation respectively.

In patients with atrioventricular block and rare heart rhythm, right ventricular electrical stimulation is applied, which might impact negatively on the structure and function of the heart. In the BIOPACE (Biventricular pacing for atrIo-ventricular BlOck to Prevent cArdiaC dEsynchronization) study [16], such patients (mean age 73.5 years) were randomized to perform right ventricular (n=908) or biventricular pacing (n=902). After an average of 5.6 years of follow-up, the time before death or hospitalization for CHF (primary endpoint) tended to decrease in biventricular pacing group (-13%; P=0.08). There was no significant reduction in the total incidence of these events in patients with LVEF ⩽50% (-8%; P=0.47) and >50% (-12%; P=0.21). Dysfunction of an expensive biventricular pacing was noted in 14.8% of cases in the absence of such problems in a right ventricular pacing.

Resynchronization therapy is recommended for patients with CHF and wide QRS complex, but the optimal area of electrical stimulation of the right ventricle is specified. The SEPTAL-CRT (Comparison of Right Ventricular Septal and Right Ventricular Apical Pacing in Patients Receiving a CRT-D Device) study [17] included patients with LVEF ⩽35% and QRS >120 ms, who were performed after randomization electrical stimulation of the right ventricle in the apex (n=92) or ventricular septal (n=90). After 6 months there were no significant differences in a reduction of LV end-systolic volume –29.3±44 and 25.3±39 mL (P=0.79), increase in LVEF, frequency of hospitalization for heart failure, total mortality – 3.0 and 3.8% (P=0.77), frequency of complications from electrical stimulation between groups of apical and septal stimulation, respectively.

Patients with persistent AF in order to maintain stable sinus rhythm are recommended not only pulmonary vein isolation but also additional ways of ablation. The STAR AF 2 (Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Part 2) study [18] after randomization performed only isolation of the pulmonary veins (n=64), isolation of the pulmonary veins and additional ablation based on the results of electrophysiological 3D-mapping (n=263), isolation of the pulmonary veins and linear ablation in the left atrium (n=259). The mean duration of catheter ablation procedure was 167, 229 and 223 mins (P<0.001) in each of the three groups. After 18 months, free from AF with duration >30 s (primary endpoint) were 59%, 48% and 44% (P=0.15) of patients, including 48%, 37% and 33% (P=0.11) of patients, respectively, without antiarrhythmic drug therapy. In patients with persistent AF, adding ablation for eliminating complex electrograms or linear ablation to pulmonary vein isolation lengthens the procedure, but does not provide the best prevention of arrhythmia recurrence. The EuroEco (European Health Economic Trial on Home Monitoring in ICD Patients) study [19] compared the cost of managing 303 patients with implantable cardioverter-defibrillators, randomized for home telemonitoring technology or traditional visits to a medical facility. Despite the higher cost of the home telemonitoring, in its application, patients required fewer doctor's visits – 3.79±1.67 vs. 5.53±2.32 (P<0.001), with a slight increase in unscheduled visits – 0.95±1.50 vs. 0.62±1.25 (P<0.005), more out of office – 1.95±3.29 vs. 1.01±2.64 (P<0.001) and Internet sessions – 11.02±15.28 vs. 0.06±0.31 (P<0.001), more

discussions in a clinic – 1.84±4.20 vs. 1.28±2.92 (P<0.03), but fewer hospitalizations – 0.67±1.18 vs. 0.85±1.43 (P=0.23) with their insignificantly shorter duration – 6.31±15.5 vs. 8.26±18.6 days. (P=0.27). As a result, the cost of home telemonitoring and traditional monitoring of patients with implantable cardioverter-defibrillators did not differ significantly.

Clinical studies presented at the scientific Hot Line IV session – Myocardial infarction

In accordance with the current recommendations, primary percutaneous coronary intervention (PCI) in patients with STEMI is limited by infarct-related artery. In the CvLPRIT (Results of the Complete versus Lesion only PRimary-PCI Trial) study [20], after randomization such patients were performed revascularization of the infarct-related only (n=146) or all arteries with hemodynamically significant stenoses (n=150). After 12 months the cumulative incidence of death from any cause, recurrent MI, heart failure and revascularization due to myocardial ischaemia (primary endpoint) was significantly lower in the group of complete revascularization – 10.0% vs. 21.2% (P=0.009). There was also observed a tendency towards a decrease of overall mortality – 1.3% vs. 4.1% (P=0.14), frequency of recurrent MI – 1.3% vs. 2.7% (P=0.39), heart failure – 2.7% vs. 6.2% (P=0.14), re-PCI – 4.7% vs. 8.2% (P=0.20) without increasing the risk of stroke, bleeding or contrast-induced nephropathy during complete revascularization.

The ATLANTIC (Administration of Ticagrelor in the cath Lab or in the Ambulance for New ST elevation myocardial Infarction to open the Coronary artery) study [21] compared the effects of earlier ticagrelor intake in the pre-hospital (in ambulance) and stationary (in a catheterization laboratory) stages of treatment of patients with STEMI. After MI diagnosis with the duration of symptoms >30 mins but <6 hours and the estimated time before PCI <120 mins, in addition to standard therapy after randomization, patients in the 'pre-hospital' group (n=909) started treatment with a loading dose of 180 mg ticagrelor and then a matching placebo when in the hospital. Patients in the 'in-hospital' group (n=953) received placebo in the ambulance, and then 180 mg of ticagrelor in the hospital on average by 31 mins later. All patients subsequently received ticagrelor 90 mg 2 times a day. There was no distinction between 'pre-hospital' and 'in-hospital' groups in the absence of ST segment depression by ≥70%–86.8% vs. 87.6% (P=0.63), blood flow in the infarct-related artery with thrombolysis in myocardial infarction (TIMI) grade 3 – 82.6% vs. 83.1% (P=0.82), amount of cardiovascular complications in the first 30 days – 4.5% vs. 4.4% (P=0.91). However, incidence of definite stent thrombosis was lower in the 'pre-hospital' group of ticagrelor treatment after 24 hours – 0% vs. 0.8% (P=0.008) and 30 days – 0.2% vs. 1.2% (P=0.02). The incidence of bleeding and serious side effects in compared groups did not differ significantly.

Treatment selection for non-ST elevation myocardial infarction (NSTEMI) in the randomized FAMOUS-NSTEMI (Fractional Flow Reserve Versus Angiographically Guided Management to Optimise Outcomes in Unstable Coronary Syndromes) trial [22] was carried out by taking into account the results of fractional flow reserve (FFR) measurement (n=176) or initially without FFR only according to coronary angiography (n=174). FFR ≤0.80 was an indication for PCI or coronary bypass surgery. The proportion of patients who initially had drug therapy was higher in the group where results of determining FFR were taken into account – 22.7% vs. 13.2% (P=0.022). Accounting for FFR resulted in a change of tactics (drug treatment, PCI or coronary artery bypass surgery) in 21.6% of patients. After 12 months revascularization rate remained lower in the group of treatment under the control of FFR – 79.0% vs. 86.8% (P=0.054). There were no statistically significant differences in indicators of health and quality of life between compared groups.

The randomized NOMI (Nitric Oxide for inhalation to reduce reperfusion injury in acute st-elevation Myocardial Infarction) study [23] included patients with STEMI without manifestations of heart failure in the first 2–12 hours after the onset of symptoms. In order to reduce damage to the myocardium before PCI and 4 hours after the reperfusion, inhalation of nitric oxide and oxygen via a face mask was performed (n=125) or was not (n=125). According to magnetic resonance imaging (MRI), 48–72 hours after the procedure, the mean infarct size was 18% vs. 19.4% of LV mass (P=0.44) in patients receiving and not receiving nitric oxide, respectively. Its positive effect on the volume of necrosis was significantly higher in patients who had not received an infusion of nitroglycerin (n=132) compared with those who received it (n=93). After 4 months in the group of patients used inhaled nitric oxide, better recovery of LV function was observed (P=0.048), there was noted a trend to a reduction of the total frequency of death, recurrent myocardial ischaemia, stroke, and rehospitalization (P=0.10).

In the MITOCARE (Effect of Intravenous TRO40303 as an Adjunct to Primary PCI For Acute STEMI) study

[24], an agent TRO40303 was evaluated in respect of reducing reperfusion injury in STEMI patients underwent revascularization. Within 6 hours of the onset of the pain syndrome, patients received intravenous TRO40303 6 mg/kg (n=83) or placebo (n=80) before the primary PCI. In both groups, no significant differences in the dynamics of creatine kinase and troponin I were observed. Also the size of the infarct was comparable according to the results of MRI – 17% vs. 15% of LV mass, LVEF in the first day – 46% vs. 48%, and after 30 days – 51.5% vs. 52.2% in the groups of TRO40303 and placebo, respectively.

Clinical studies presented at the scientific Hot Line V session – Coronary artery disease and atrial fibrillation

According to the results of small randomized studies, perioperative statin therapy reduced the likelihood of developing AF after cardiac surgery, and also prevented damage of myocardium and kidneys. In the STICS (Statin Therapy In Cardiac Surgery) study [25], 8 days before and 5 days after elective heart surgery, rosuvastatin 20 mg/day (n=960) or placebo (n=962) were used. The incidence of AF was 21% vs. 20% (*P*=0.72) in the groups of rosuvastatin and placebo, respectively. In both groups, there were no significant differences in plasma levels of troponin I (*P*=0.72), reflecting perioperative myocardial injury, duration of hospitalization, cardiac and cerebrovascular complications during hospitalization, LV function by echocardiography, and plasma creatinine levels.

In the X-VeRT (eXplore the efficacy and safety of once-daily oral riVaroxaban for the prevention of caRdiovascular events in patients with nonvalvular aTrial fibrillation scheduled for cardioversion) study [26], rivaroxaban (20 mg once a day or 15 mg for creatinine clearance of 30-49 mL/min) (n=1,002) and adjustable dose warfarin (n=502) were compared in patients with AF lasting >48 hours, undergoing cardioversion. Subject to prior anticoagulation or exclusion of thrombosis in the atria according to transesophageal echocardiography, early (after 1-5 days after randomization) and in other cases delayed (after 3–8 weeks) cardioversion was performed. The overall incidence of stroke, transient ischemic attack, peripheral embolism, MI and cardiovascular death (primary efficacy endpoint) was 0.51% and 1.02% in the groups of rivaroxaban and warfarin (relative risk (RR) 0.50, 95% confidence interval (CI) 0.15–1.73). Major bleeding was recorded at a frequency of 0.6% and 0.8% when taking rivaroxaban and warfarin, respectively (RR 0.76, 95% CI 0.21–2.67). Therefore rivaroxaban is an effective, safe and convenient alternative to warfarin during cardioversion of AF.

In the first months after catheter ablation of AF, recurrences of arrhythmias are often observed, but long-term effects of a short-term antiarrhythmic drug therapy are not well studied. In the AMIO-CAT trial (Recurrence of arrhythmia following short-term oral AMIOdarone after CATheter ablation for atrial fibrillation: a double-blind, randomized, placebo-controlled study) [27] after pulmonary vein isolation, supplemented by linear ablation, amiodarone (800 mg/day for 2 weeks; 400 mg/day during 3rd and 4th week; 200 mg/day from 5th to 8th week, n=108) or placebo (n=104) were applied in patients with paroxysmal or persistent AF. Registered episodes of AF lasting >30 seconds during 4-6 months after ablation were observed in 39% and 48% of patients in the placebo and amiodarone groups, respectively (*P*=0.18). In the first 3 months after ablation, patients, receiving amiodarone, had significantly lower recurrence rate of AF – 34% vs. 53% (*P*=0.006), arrhythmias which required hospitalization (*P*=0.006), and cardioversion (*P*=0.0004). Despite the side effects of amiodarone, due to antiarrhythmic action, it ultimately did not reduce patients' quality of life (according to the SF-36 questionnaire).

The effect of a long-term, high-intensity statin therapy on coronary atherosclerosis in STEMI patients remained unknown. In the IBIS 4 (Integrated Biomarkers and Imaging Study-4) study [28], the effect of rosuvastatin at a dose of 40 mg/day on plaque size and phenotype in two non-infarct related epicardial arteries, according to intravascular, including radiofrequency, ultrasound, was evaluated in 103 STEMI patients. After 13 months LDL levels decreased from 3.29 to 1.89 mmol/L (*P*<0.001), high-density lipoprotein (HDL) levels increased from 1.10 to 1.20 mmol/L (*P*<0.001), and the amount of plaque was reduced by 0.9% (*P*=0.007). The proportion of patients with plaque regression in at least one artery was 74%. There were no significant changes in the amount of necrotic core of plaque (-0.05%; *P*=0.93) and number of radio frequency ultrasonic slices revealed thin covering of plaque (*P*=0.15).

Tuberculous pericarditis is associated with high morbidity and mortality, even on the background of antituberculous treatment. The IMPI (Investigation of the Management of Pericarditis) trial [29], using a 2×2 factorial design, assessed the impact of 6 weeks of adjuvant prednisolone therapy (initial dose of 120 mg/day with a reduction to 5 mg/day) and immunotherapy with Mycobacterium indicus pranii (5 injections for 3 months) in 1,400 patients with tuberculous pericar-

ditis. Two-thirds of the trial participants had the human immunodeficiency virus detected. The incidence of the primary endpoint (death, pericardial tamponade or constrictive pericarditis) was not significantly different in patients treated with prednisolone or placebo – 23.8% vs. 24.5% (*P*=0.66), as well as in those receiving immunotherapy or placebo – 25.0% vs. 24.3% (*P*=0.81). Prednisolone, compared with placebo, significantly reduced the incidence of constrictive pericarditis – 4.4% vs. 7.8% (*P*=0.009). Both prednisolone therapy and immunotherapy, compared with placebo, significantly increased incidence of cancer – 1.8% vs. 0.6% (*P*=0.03) and 1.8% vs. 0.5% (*P*=0.03) respectively, which was explained by the influence of HIV infection.

The next European Society of Cardiology Congress will be held between 29 August and 2 September 2015 in London (UK).

Conflict of interest: None declared

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