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Contents

INTERVENTIONAL CARDIOLOGY

Does intracoronary injection of phosphocreatine prevent myocardial reperfusion injury following angioplasty of infarct-related artery in acute-stage of myocardial infarction?
D.G. Iosseliani, A.G. Koledinsky, N.V. Kuchkina 10

Our initial experience with endovascular occlusion of patent ductus arteriosus and transcatheter closure of atrial septal defect.
T.V. Kislukhin, V.V. Goryachev, N.V. Lapshina, S.E. Shorokhov, N.I. Knizhnik, A.V. Gorbacheva, E.A. Suslina, E.M. Blagochinnova, S.M. Khokhlunov. 15

Causes of in-stent restenosis
I.V. Pershukov, T.A. Batyraliev, A.N. Samko, Z.A. Niyazova-Karben, I.V. Levitsky, F.Besnili, T.Suleimanova, A.Guven.....20

Immediate and mid-term angiographic outcome of coronary stenting with BX stents (Sonic and Velocity) (Cordis, Johnson & Johnson) in patients with CHD. A single-center study.
S.P. Semitko, D.G. Gromov, A.G. Koledinsky, I.S. Topchian, P.Yu. Lopotovsky, D.G. Iosseliani.....25

EXPERIMENTAL CARDIOLOGY

Regression of Coronary Artery Lesions Triggered By Electric Pacing.
M.Mouanoutoua, S. Allaqaband, R. Tumuluri, E. M. Mortada, Y. Shalev, FACC, A. Gupta, T. K. Bajwa, M. Akhtar, V. Chekanov. 29

CLINICAL CASES

Coronary artery aneurysm: three case reports.
S.A. Abugov, V.A. Sulimov, A.E. Udovichenko 34

LEADING RUSSIAN CENTERS OF INTERVENTIONAL CARDIOANGIOLOGY

Ulyanovsk regional clinical hospital, Department of Interventional radiology 37

ABSTRACTS OF THE 5TH INTERNATIONAL SYMPOSIUM "CARDIOVASCULAR AND INTERVENTIONAL RADIOLOGY" (Center of Endosurgery and Lithotripsy, in cooperation with Russian Society of Interventional Cardioangiology, Russian Society of Angiology and Vascular Surgery, All-Russian Society of Cardiology, Russian Society of Obstetrics and Cynecology, Moscow City Center of Interventional Cardioangiology. Moscow, April 22-24, 2004). (End, for the beginning see N5-2004).....38

Does intracoronary injection of phosphocreatine prevent myocardial reperfusion injury following angioplasty of infarct-related artery in acute-stage of myocardial infarction?

D.G. Iosseliani, A.G. Koledinsky, N.V. Kuchkina[1]

Complete cessation of flow in certain myocardial region resulting from acute coronary artery occlusion now is considered to be a definite and important pathogenic factor in AMI, i.e. the ischemic necrosis of myocardium (1). The first signs of myocardial cells decomposition are reported to occur as early as 20 to 40 minutes following the cessation of flow in the coronary artery (3). These signs include gradual loss of glycogen, swelling of mitochondria, destruction of sarcoplasmatic reticulum and mitochondria. Signs of ischemic myocardial necrosis that occur at the biochemical level include dramatic reduction of oxidative phosphorylation and parallel accumulation of anaerobic glycolysis products, particularly lactate, in the muscle tissue (2). Other events that develop simultaneously include: accumulation of non-esterified fatty acids, gradual release of potassium ions from the cells, and accumulation of calcium ions within the damaged mitochondria and myofibril cytoplasm due to the sharp decrease of myocardial cell energy source (3). Therefore, accumulation of lactate, non-esterified fatty acids, and calcium ions initiate the vicious circle, which aggravates ischemia and extends the area of necrosis. Thus, absolutely microscopic necrotic changes of myocardium occurring within the first hours after cessation of flow in the coronary artery give rise to macroscopic areas of necrosis 10-12 hours later indicating the extension of necrotic process (4,5).

In brief, this is the mechanism of myocardial injury after AMI caused by acute occlusion of the coronary artery, which supplies blood to appropriate myocardial region. This explains why for many years investigators are trying to find the quickest and the most effective way to restore blood flow in the coronary artery in order to stop coagulation necrosis and myocytolysis of myocardium.

Clinicians are currently armed with three methods of blood flow restoration in the occluded coronary artery. The first and the most commonly used method is medical therapy with systemic or intracoronary thrombolysis ensuring partial restoration of blood flow in the coronary artery due to thrombus destruction. The second and substantially more aggressive method is surgical revascularization of myocardium, which provides reestablishment of blood flow in the infarct-related artery by means of bypass grafting of the occluded artery. And finally, the third method, which is thought to be the most effective - primary angioplasty and stenting of the infarct-related artery (IRA) providing the most complete restoration of coronary artery patency (6).

However, some authors believe that blood flow restoration in the IRA (i.e., myocardial reperfusion) contributes to further damage of myocardium due to the lack of endogenous energy sources and the entry of calcium ions and anaerobic glycolysis products into the damaged cells. As a result, persistent muscle fiber contracture develops (3). This negative process manifests by the increased blood levels of myocardial injury markers such as creatine phosphokinase and lactate dehydrogenase, as well as myocardial cell injury marker protein - troponin I (7).

The substantial (sometimes 10-fold) increase of cardiospecific enzymes following AMI is proposed by some authors to be an indicator of blood flow restoration after acute coronary artery occlusion, i.e. the marker of myocardial reperfusion. In order to prevent the undesirable effect of infarction area reperfusion many investigators attempted to use cardioprotective agents administered intravenously to preserve viability of myocardial cells (8,9). A particular method is systemic intravenous administration of high-energy phosphocreatine within the first hours after acute myocardial infarction. Yet, very high bioavailability and elimination coefficient make the probability that an appropriate amount of phosphocreatine will get into the infarction area doubtful. On the other hand, when introduced directly into the recanalized IRA the compound would apparently be more effective and exhibit its effect in appropriate concentration upon the affected myocardium. Unfortunately, this is still merely an assumption, as we have failed to find any published data. This has become the soil for our study, which was designed to investigate the efficacy of intracoronary administration of high energy phosphocreatine within the first hours of acute myocardial infarction to prevent death of myocardial cells following reperfusion in AMI patients.

Clinical data of patients and study methods.

The study enrolled 20 patients, who underwent selective coronary angiography, left ventriculography, recanalization and angioplasty of the IRA within the

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first 6 hours following the infarction. The size of myocardial infarction after acute occlusion of circumflex artery or the right coronary artery varies greatly with the type of coronary blood supply, whereas LAD occlusion leads to a more homogeneous appearance of myocardial infarction. Therefore, we selected patients with acute occlusion of proximal LAD before the origin of first order branches and TIMI 0 antegrade flow to allow for more objective comparison. Another mandatory inclusion criterion was the successful recanalization of the IRA and successful PTCA. After successful PTCA of infarct-related artery patients were randomly assigned to the group of intracoronary creatinephosphate administration or the control group.

Intracoronary administration of Neoton phosphocreatine (ALFA WASSERMANN) was started after the first dilation of the IRA in a dose of 0,5 g dissolved in 20 ml of normal saline. On completion of the procedure 3-min intracoronary administration of the remaining dose (1.5 g) was performed with maximum volumetric injection speed of 4 ml/sec.

Blood was sampled (5 ml from the cubital vein) to investigate the level of myocardial cell injury markers (troponin I, myoglobine) in accordance with the appropriate guidelines during recanalization, 12 and 24 hours following the procedure (13,14). After 15-min incubation the blood was centrifuged at 4000 rpm for 10 min. The serum was stored at -20°C. Serum troponin I and myoglobin were quantified by enzyme immunodetection using monoclonal antibodies to myoglobin and cardiac isoform of troponin I (Myoglobin ELISA, Troponin I ELISA, DRG Instruments GmbH, Germany) and E-Liza Mat-3000 microplate photometer (DRG International Inc., USA) at 450 nm wavelength. Sensitivity of these diagnostic sets for myoglobin and troponin I detection was 5.0 ng/ml and 1.0 ng/ml, respectively; the increase of troponin I over 1.5 ng/ml and myoglobin over 90 ng/ml after myocardial injury was considered diagnostically relevant.

Results.

Table 1 shows baseline clinical and laboratory values of the patients examined.

The table shows that the majority of patients were smokers with hypertension and lipid metabolism disorders (over 60% of cases). Most of patients were men.

Table 1. Baseline clinical data, medical history and laboratory values of the groups studied.

	Group 1 (neoton)	Group 2 (control)	p
Mean age (years)	55±8	57±11	ns
Men (%)	90±31	100	
Arterial hypertension (%)	60±50	60±50	
Smoking (%)	70±48	60±50	
History of CHD (months)	10±4	8±5	
Hypercholesterolemia (mol/l)	60±50	70±48	
Hypertriglyceridemia (mol/l)	50±52	50±52	ns
LVEF (%)	48±4	45±5	
Heart failure (%)	40±51	30±48	

No patient had a history of AMI, i.e. they suffered their first AMI.

Mean time to hospital admission was 4.7 hours after the beginning of chest pain in group 1 and 4.5 hours in group 2 (range 1.5 - 5 hours), the difference was not statistically significant. All patients had ECG sogns of Q-wave in V1-V5, V6 accompanied by ST elevation in the same leads. On admission 3 (30%) patients in group 1 and 4 (40%) patients in group 2 had frequent single or paired ventricular extrasystoles. Three (30%) patients in group 2 and 2 (20%) patients in group 1 had intraventricular conductive disorders (partial left bundle-branch block).

Left ventricular ejection fraction according to left ventriculography was 45+5%. Mean values of global and segmental left ventricular contractility in the groups studied are summarized in the Table 1 and Figures 1, 2).

The graphs show that akinesia of anterolateral and apical LV segments was observed most commonly.

At the same time, the intact LV segments (anterobasal, diaphragmatic, and posterobasal) developed compensatory hyperkinesia, which returned to normal level after 1-2 weeks as shown by echocardiography. Immediately after selective coronary angiography the patients underwent interventional endovascular procedure (balloon angioplasty and/or stenting of IRA). Some clinical and angiographic values in the groups

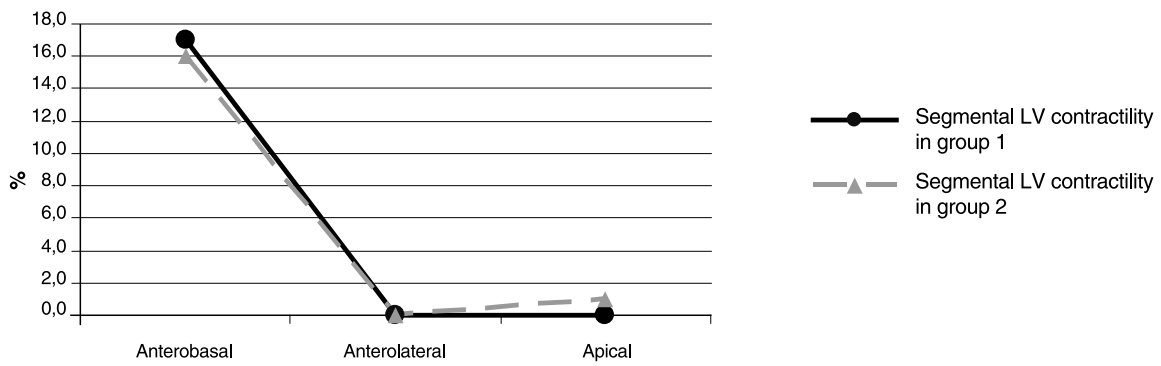

Figure 1. Contractility of anterior segments of the LV.

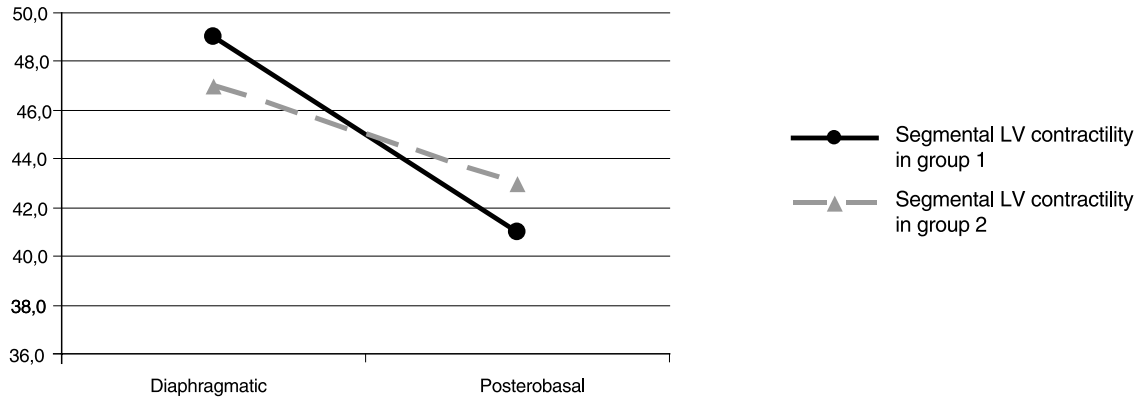

Figure 2. Contractility of posterior segments of the LV

Table 2. Baseline clinical, angiographic, and procedural values.

	Group 1	Group 2	p
Mean vessel diameter (mm)	3.5±0.3	3.3±0.4	ns
Mean length of occlusion (mm)	23±6	24±6	
Mean number of affected arteries	1.3±0.3	1.2±0.4	
Collateral pathways (%)	10%	0%	
Balloon predilatation (%)	100%	100%	
Mean time of procedure (min)	67±11	71±12	
Mean time of fluoroscopy (min)	20.9±6.8	18.3±5.9	
Mean volume of contrast medium (ml)	327±56	348±69	
Angiographic success (%)	100%	100%	
Complications of the procedure (%)	0%	0%	
Mortality (%)	0%	0%	

studied are shown in Table 2).

Intrasystemic and intersystemic collaterals were absent in 95% of patients. A single patient of group 1 had grade 1 collateral blood flow into the distal part of the occluded artery via intersystemic collateral pathways. PTCA was performed 5.1±0.5 hours and 4.9±0.4 hours after the beginning of chest pain in group 1 and group 2, respectively (statistically nonsignificant difference). PTCA was successful in all patients: there was no threat of dissection, distal embolization or antegrade flow deceleration. Mean volume of contrast medium used was practically similar between groups. Recanalization of the coronary artery was performed with hydrophilic guidewire. Adequate measurement of angiographic parameters of occlusion was performed after 1.5-2.0 mm balloon predilatation. The lesion of target artery was assessed with digital subtraction angiography for the appropriate choice of balloon diameter and the achievement of angiographic success. The patients were followed-up in ICU during 1-2 days after the procedure and subsequently reallocated to cardiology department.

All patients studied were stable during hospital stay and no major complications were observed. The patients received treatment according to local guidelines. There were no differences between groups in antianginal agents used prior to hospitalization (see Table 3).

Disaggregant therapy after successful endovascular procedure was standard: 500 mg/day ticlopidine during 1 month and permanent administration of 100 mg/day aspirin.

One week following endovascular procedure all

Table 3. Medical therapy in the groups studied (%).

Pharmacological group:	Group 1	Group 2	p
Nitrates	90±31	80±42	ns
β-blockers	80±42	80±42	
Calcium channel inhibitors	50±52	40±51	
Antianginal agents:			
of a single group	0%	0%	
of two different groups	60±50	70±48	
of three different groups	40±51	30±48	

patients underwent repeated echocardiography study and exercise tolerance test was performed 10 days after the procedure unless there were any contraindications. Exercise tolerance test wasn't conducted in patients with aneurysm of the anterior LV wall. Results of these studies are shown in Tables 4,5.

Therefore, LVEF measured by echocardiography remained unchanged in group 1 as compared to base-

Table 4. LV contractility in the groups as measured by EchoCG.

	Group 1	Group 2	p
LVEF (%)	47±8	35±7	<0,05
LV aneurysm (patients)	2	6	

line values, whereas in group 2 the EF value was decreased by 12% on average ($p<0.05$, significant difference). LV aneurysm was found in 2 patients of group 1 vs. 6 patients in group 2, so this complication was significantly more common in group 2 ($p<0.05$).

As shown in the table, exercise tolerance was measured in 8 patients of group 1 and 4 patients of group 4. A higher exercise tolerance was observed in

Table 5. Results of bicycle ergometry in the groups studied.

	Group 1	Group 2	p
Number of patients	8	4	
Mean exercise tolerance (W)	94±16	50±20	ns

group 1, however, this difference was not significant due to small number of patients.

Some studies of blood components are known to provide important information of both qualitative and quantitative parameters of myocardial ischemic injury (10). The most important of these are troponins - proteins located on fine myofilaments of myocardial cell

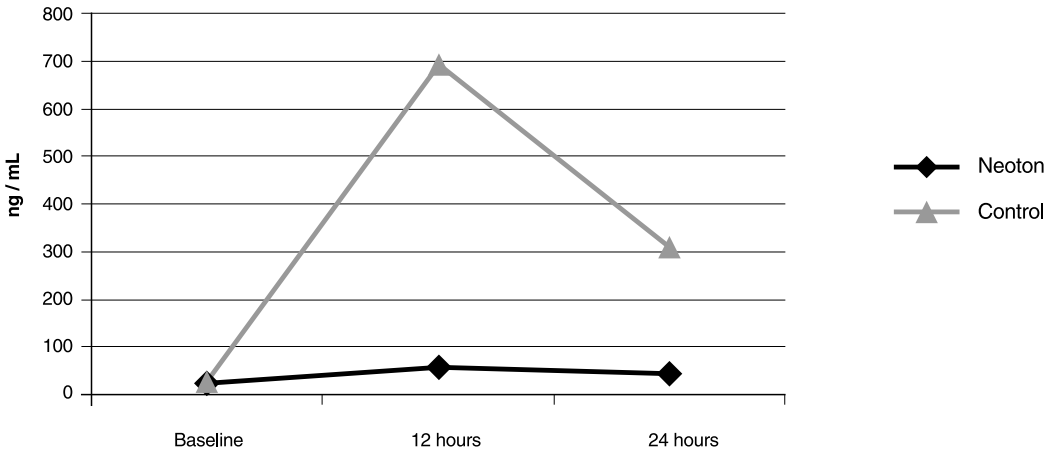

Figure 3. Changes of troponin I level in the groups studied

contractile system. Troponin complex consists of three components - troponins C, T, I. Cardiac troponins (T and I) are the specific markers of myocardial cell injury and have similar sensitivity and specificity (11,12). Minimal time to troponin increase following IRA occlusion is 4 to 6 hours (12,13). The first blood sample for myocardial injury markers study was taken during IRA recanalization. Troponin I concentration ranged from 0 to 20 ng/ml with the mean value of 9±5 ng/ml in group 1 vs 13±6 ng/ml in control group (statistically nonsignificant difference). As the purpose of our study was to assess the role of intracoronary creatinephosphate administration in reperfusion injury of myocardial cells following PTCA of IRA for acute-stage myocardial infarction, the second time-point for blood sampling was defined as 12 hours, when the troponin level peaks after IRA reperfusion (13,14). The third time-point was at 24 hours. Values of the marker protein concentration significantly differed between the groups studied ($p<0.05$), (see Figure 3).

The above figure shows, that troponin I level was more than 10 times lower in group 1 as compared to control group ($p<0.05$) indicating less myocardial cell injury (15), whereas in group 2, as expected, cardiac markers increased due to reperfusion injury of myocardial cells suggesting blood flow restoration in IRA (7).

A sensitive marker of non-specific myocardial injury is myoglobin. Changes of myoglobin concentration as the earliest biochemical marker of AMI are shown in the Figure 4.

Baseline myoglobin level was similar between groups (no statistically significant difference was found, $p>0.05$), whereas at the second time-point there was a trend towards the decrease of myoglobin in group 1 compared to group 2 ($p>0.05$).

Conclusion.

Numerous drugs and methods are used for myocardial protection during acute ischemia and infarction with phosphocreatine being one of the major ones. Administration of phosphocreatine is known to have favorable effect on infarction area limitation during both acute ischemia and myocardial infarction (15,16). The latter is due to high cardioprotective effects of the drug mediated by stabilization of myocardial cell sarcolemma, inhibition of hypoxemic myocardial contraction, improved microcirculation within the infarction zone, prevention of ischemic and reperfusion injury. However, all investigators used systemic (intravenous) administration of the drug. Considering the pharmacodynamics of creatinephosphate pharmaceutical form one can assume, that the amount of active substance that gets into the necrosis area is small, because due to the occlusion of coronary arteries carrying blood to the infarction area, the drug would only enter this focus by collateral pathways, if at all. Thus, intracoronary administration

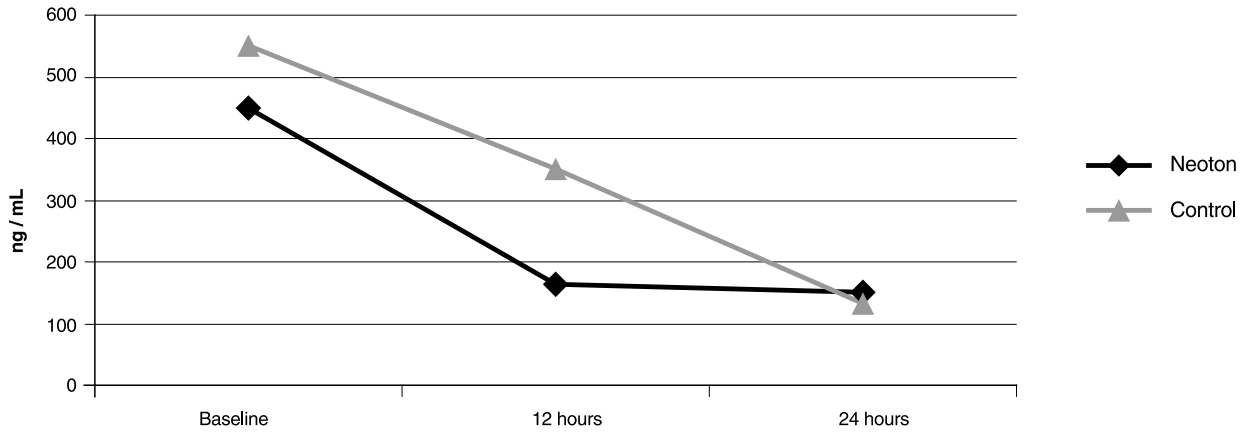

Figure 4. Changes of myoglobin level in the groups studied

immediately after recanalization of the infarct-related artery was proposed to limit the infarction area and decrease reperfusion injury. As a result, more than 10-fold significant decrease of troponin I (a specific marker of myocardial cell necrosis) was obtained in group 1 with intracoronary phosphocreatine administration as compared to the control group. In addition, intracoronary administration of phosphocreatine was associated with more favorable clinical course during hospital stay in this group of patients.

In conclusion, this study suggested possible positive effect of intracoronary phosphocreatine administration on myocardial reperfusion injury and prevention of hybernating myocardium necrosis following restoration of antegrade flow in the infarct-related coronary artery during the first hours after AMI. Further studies are necessary to confirm this preliminary experience.

References:

1. A.N. Strukov, V.V. Serov. Human pathology. Moscow, Meditsina publishers, 1993, 98.
2. N. Spirilakis. Physiology and pathophysiology of heart. Moscow, Meditsina 1988; 2: 348-349.
3. M.V. Bilenko. Ischemic and reperfusion injury of organs. Moscow. Meditsina, 1989.
4. Syrkin A.L. Myocardial infarction. Moscow. Meditsina, 1991: 38-40.
5. O.V. Korpacheva, R.V. Viskov et al. Pathogenesis and clinical pattern of emergency conditions. 1998. Omsk. Proceedings of the research and training conference.
6. D.G. Ioseliani, A.A. Filatov, S.V. Rogan et al. Restoration of flow in the infarct-related artery in acute myocardial infarction: effective or spectacular? International Journal of Interventional Cardioangiology, 2003 1: 33.
7. Quantification of creatine kinase MB isoenzyme. MI J Am Coll Cardiol 1998; 31; 1499-505.
8. The EMIR-FR GROUP. Effect of 48-h intravenous trimetazidine on short- and long-term outcome of patients with acute myocardial infarction, with and without thrombolytic therapy. Eur. Heart J., 1000,21,1537-1546.
9. M.V. Bilenko. Theoretical and experimental basis for antioxidant therapy to prevent acute ischemic injury of organs. Nauka, 1982: 195-213
10. Ravkilde J., Horder M., Gerhardt W. et al. The predictive value of cardiac troponin T in serum of patients suspected of acute myocardial infarction. Scand. J. Clin. Invest. 1993; 53: 677-85
11. Plebani M, Zaninotto M. "Diagnostic strategies in myocardial infarction using mioglobin measurment" Eur.J.Cardiol. - 1998 - 19(Suppl. N);N12-15.
12. Chapelle J.P. "Cardiac troponin J and troponin T: recent players in the field of myocardial markers" Clin. Chem. Lab. Med. - 1999: 37(1): 11-20
13. M.B. Filippenko, I.I. Staroverov et al. Detection of cardiac troponin T and creatine kinase mass in the diagnosis of acute myocardial infarction. Kardiologia, 2001; 3: 17-20.
14. Katus H.A, Remppis A, Scheffold T, et al. "Intracellular compartmentation of cardiac troponin T and its release kinetics in patients with reperfused and nonreperfused myocardial infarction" Am. J. Cardiol. - 1991 - 67(16): 1360-1367.
15. A.P. Golikov, V.A. Riabinin, V.A. Pavlov et al. Therapeutic potential of phosphocreatine in acute myocardial infarction. Cardiologia, 1987; 5: 50-53
16. A.P. Golikov, V.A. Riabinin, P.P. Golikov et al. Efficacy of emoxilin and neoton in unstable angina. Terapevtichesky arkhiv, 1996; 1: 33.
17. Stewart J.T., French J.K. et al. Early noninvasive identification of failed reperfusion after thrombolysis in acute MI. J Am Coll Cardiol 1998;31:1499-505.

Our initial experience with endovascular occlusion of patent ductus arteriosus and transcatheter closure of atrial septal defect.

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Patent ductus arteriosus (PDA) is one of the most common congenital heart diseases According to various authors its rate ranges from 11% to 20% of all congenital heart diseases [4]. During the first year of life the mortality with natural course of PDA comes to 30%. Subsequently the cumulative mortality rate makes 0.5% per year and comes to 2-4% per year by 20 years (22). Average life span of patients with PDA is around 40 years. Patients who have undergone surgical treatment of PDA have the longer life span and better hemodynamics. Mortality rate after surgical correction of patent ductus arteriosus is less than 0.5% (1). The degree of aorta-pulmonary artery shunt depending on duct diameter and pressure difference between aorta and pulmonary artery (PA) is the main aspect of pathogenesis of this heart defect. Functioning PDA produces the excess pulmonary blood flow and progressively leads to pulmonary hypertension and pulmonary vascular obstructive disease.

Atrial septal defect (ASD) is no less common heart defect than PDA, with the rate of 5-15% (3) of all congenital heart diseases. In non-operated patients with moderate ASD average life span ranges from 30 to 40 years, however in the third decade of life the heart defect is complicated by atrial fibrillation in 30% of patients. Mortality rate during surgery for this heart defect is less than 1% (1).

Mild shunt relative to ASD leads to moderate right heart volume overload, so PA pressure can remain normal. However, severe pulmonary hypertension may develop, resulting in right ventricular failure.

We report our initial experience with the procedures of endovascular occlusion of PDA and transcatheter closure of ASD performed in Samara Regional Clinical Cardiology Dispensary.

Materials and methods.

Procedures of PDA occlusion in 20 patients and transcatheter ASD closure in 6 patients have been performed in Samara Regional Clinical Cardiologic Dispensary from December, 2002 till January, 2004.

Age of patients with PDA (12 females, 8 males) ranged from 2 months to 18 years (tab. 2). Mean age of patients was 3.6 years.

Table 1. Patients' distribution according to pathology and occlusion method.

Pathology	Occlusion with Cook coil	Occlusion with Amplatzer system
PAD	18	2
ASD		6

Patients with ASD (4 females, 2 males) were aged between 3 to 51 years (tab. 3) with the mean age of 9 years.

Table 2. PAD patients' number and age.

Age	Number
under 1 year	2
1-3	10
3-10	6
10-18	2

All 20 patients had isolated PDA, one of them had recanalization after surgical ligation. Patients with centrally located ASD secundum formed the ASD group.

Table 3. ASD patients' number and age.

Age	Number
1-3	
3-10	4
10-18	1
Over 18 years	1

Systolic murmur was heard on auscultation in 8 patients with PDA, and systolic-diastolic murmur over the second and third intercostal spaces at the left of the sternum - in 12 patients. The signs of right heart overload and left ventricular hypertrophy were observed on ECG in all patients with PDA. Chest X-ray revealed increase in the caliber of pulmonary vasculature, bulging of the pulmonary artery. Echocardiography included evaluation of the diameter of pulmonary end of the duct, its length, aortic ampulla dimensions. Systolic-diastolic gradient reflecting the pressure in the pulmonary artery was also evaluated. The less is the gradient, the higher is the pressure in the pulmonary artery. The pressure in the pulmonary artery was normal in 19 patients. Signs of pulmonary hypertension were detected at echocardiography in

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one patient with large PDA and were confirmed by right heart catheterization.

Systolic murmur was heard over the second intercostal space at the left of the sternum in all 6 patients with ASD. The signs of right heart hypertrophy in 2 patients and right heart overload in 4 patients were observed on ECG. In patients with ASD chest X-ray examination revealed right atrial and right ventricular enlargement, dilatation of the pulmonary artery and increased pulmonary vasculature related to hypervolemia. Average pressure in the PA according to echocardiographic data amounted to 20-25 mm Hg in 5 patients, to 45-50 mm Hg - in 1 patient; diastolic gradient on PA ranged from 5 to 14 mm Hg. Evaluated Qp/Qs ratio ranged from 1.3 to 2.3. Defect dimensions were measured from the subcostal and apical four-chamber views.

Diagnostic examination and surgical treatment were performed simultaneously in the X-ray operation room equipped with angiographic unit "Integris 5000H" ("Philips", Holland). Intervention was performed under general or local anesthesia, depending on the age of the patient.

Aortography in the left lateral view using Pigtail catheter were performed in patients with PDA. Heparin (100 units per kg body weight) was given after 4 or 5 F introducer insertion to prevent femoral artery thrombosis. Duct diameter and anatomy were assessed according to angiographic classification devised by A. Krichenko et al. [11]. Type A ductus was observed in 11 patients, type C - in 9 patients. The measurements of the pulmonary end diameter, aortic infundibulum and duct length were performed.

Embolisation coil diameter was chosen so that it should be no less than twice as large as narrowest width of the duct. The coils with 4 or 5 loops were used

Table 4. Duct diameter according to aortography.

Duct diameter	Number of patients
Less than 2 mm	12
Within 2-4 mm	6
Over 4 mm	2

depending on the length of the duct and size of infundibulum . PA trunk was catheterized with the Multipurpose or Cobra selective catheter introduced from the aorta through the PDA and embolization coil was implanted through the catheter. Occlusion was performed in such a way that 1.5-2 loops of the coil should be placed at the pulmonary site and the rest loops - inside the aortic ampulla. After the checking of the security of the anchorage, the coil was detached from the delivery system. The effectiveness of occlusion was assessed by control aortography 5-15 minutes later. Additional coil was implanted if there was residual shunt. The instruments were removed from the artery, hemostasis was secured by compression within 10-20 minutes and then the patient was transferred to the ward.

PDA occlusion with Amplatzer device, besides arterial approach, requires also venous approach (6 or 7 F

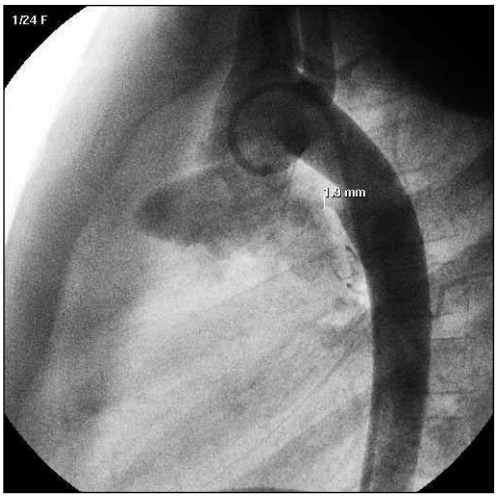

Figure 1. Patient T., 3 years. Thoracic aortography in the lateral projection. Patent arterial duct (type A) diameter 1.9 mm.

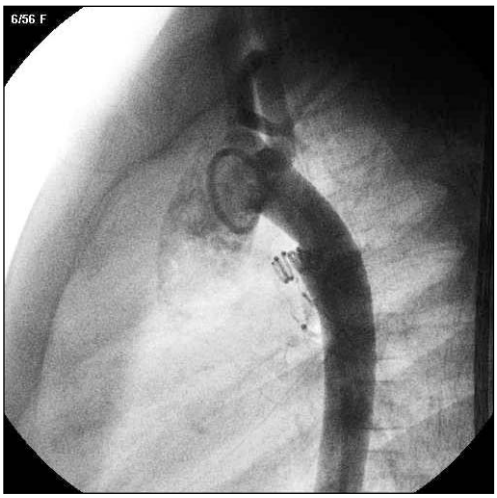

Figure 2. Patient T., 3 years. Thoracic aortography in the lateral projection after coil embolization. No shunt from aorta to PA trunk.

introducer).

Catheterization of the descending aorta was performed through the PDA from the PA trunk, using Multipurpose catheter. The diameter of the duct was measured by special sizing balloon (provided in the kit for PDA occlusion) through the 0.0035" 260 cm length guidewire. Occluder size was chosen to be 1-2 mm wider than PDA diameter evaluated during balloon sizing. The replacement of balloon by Amplatzer delivery system in the descending aorta was performed over the same guidewire. Occluder was screwed to the fixator, and then was retracted into the loader while being immersed into physiologic solution. Occluder was introduced into the aorta through the delivery device, and then the aortal disc was deployed. Disc anchorage in aortic ampulla was obtained by retrograde traction, then the delivery device was withdrawn, main part of the occluder deployed in the duct. Adequacy of occluder implantation was checked by aortography performed without detaching fixator from the occluder. Residual shunt from aorta to PA trunk was not considered to be

a contraindication for fixator unscrewing as Amplatzer occlusion efficacy According to International Protocol, residual shunt could be assessed within one year. The next day after the occlusion control echocardiography was performed, which confirmed absolute absence of shunting to PA.

Occlusion was performed with the self-centering

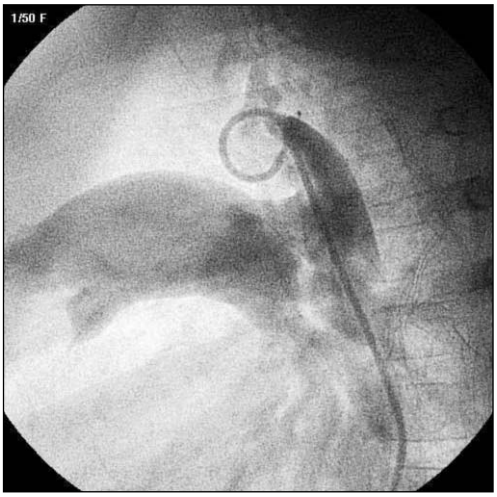

Figure 3. Patient Sh., 3 years. Thoracic aortography in the lateral projection. PAD seen in the typical location Ж 7.3 mm.

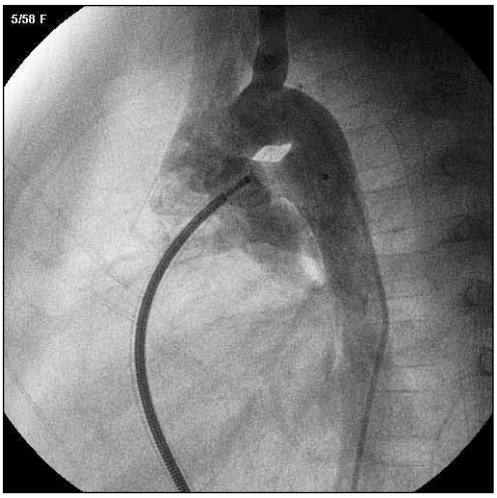

Figure 4. Patient Sh., 3 years. Thoracic aortography performed to verify "Amplatzer" occluder position.

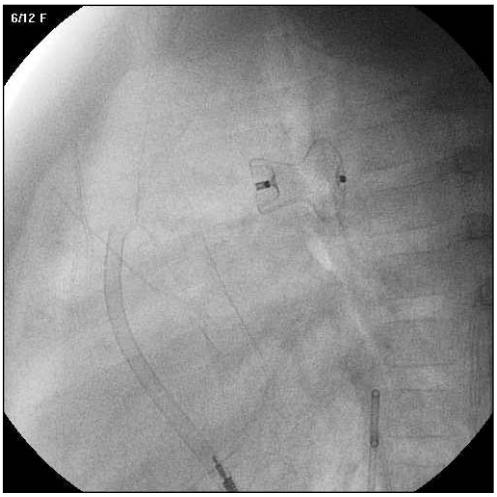

Figure 5. X-ray of patient Sh., 3 years, with implanted "Amplatzer Duct Occluder" device.

AmplatzerT Septal Occluder (AGA Medical Corporation, USA) in all 6 patients with ASD. The puncture of right common femoral vein, and then right heart catheterization with intracardiac pressure monitoring was performed using the Multipurpose catheter. The left atrium was catheterized through the ASD and 0.0035" 260 cm guidewire was inserted into the left upper lobe pulmonary vein. Exact measurements of the ASD were performed using special sizing Amplatzer balloon and the obtained data were compared with the transthoracic echocardiography data. Inaccuracy of noninvasive method ranged from 28 to 41% (table)

Preassembled AmplatzerT Septal Occluder was

Table 5. Comparison of the results of ASD sizing.

EchoCG ASD sizing data (mm)	10	11	12	15	17	33
ASD balloon sizing data (mm)	17	17	19	21	21	38

delivered to the implantation site through the delivery system inserted into PA after balloon removal. The left disc of occluding device was deployed in the left atrium under X-ray and echocardiographic guidance. Adequacy of the left disc anchorage with the defect rim was checked by retrograde traction, then disc location against the mitral valve was assessed by echocardiography and the right disc was deployed in the right atrium. Once more the adequacy of occluder position against vena cava and pulmonary vein orifices, coronary sinus and atrioventricular valves was verified by echocardiography. Having ensured the security of the anchorage, the occluder was detached from the delivery device. The appliances were removed from the vein, and the patient was transferred to the ward.

Results.

PDA occlusion was successful in all 20 patients. A single coil for PDA closure was used in 16 patients, 2 coils - in 1 case, and 3 coils - also in 1 case. Amplatzer device for duct closure was used in 2 patients. Immediate complete duct occlusion confirmed by aortog-

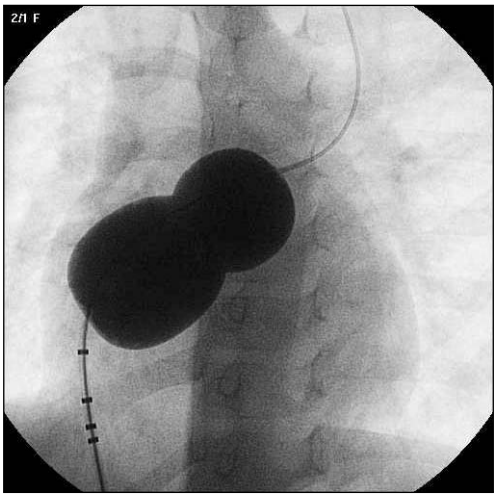

Figure 6. Patient M., 3.5 years. Sizing balloon placed in the ASD.

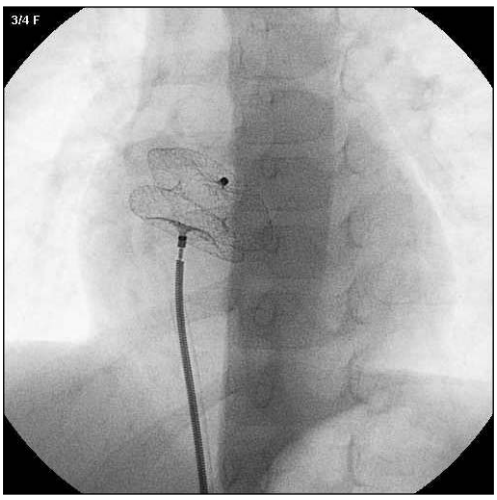

Figure 7. Patient M., 3.5 years. "Amplatzer" occluder placed in the defect. Echocardiographic assessment of the correctness of the device location against caval and pulmonary vein orifices, coronary sinus, atrioventricular valves.

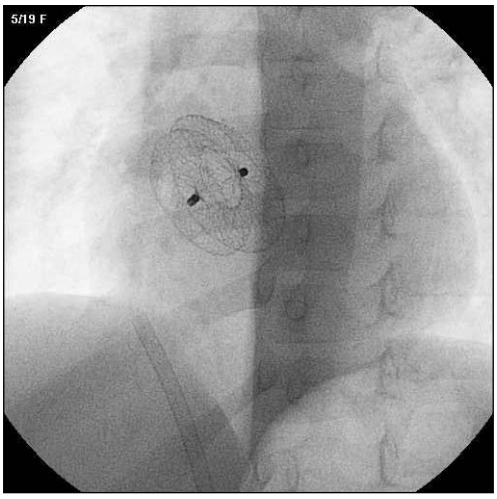

Figure 8. X-ray of patient M., 3.5 years, with implanted "Amplatzer Duct Occluder" device.

raphy performed 5-15 minutes after the procedure was observed in 16 patients. Residual shunt persisted in 4 patients, one of them had 3 coils implanted, one - 1 coil, and Amplatzer device was implanted in 2 patients. All patients with residual shunt underwent control echocardiography at 3, 12 and 24 hours postprocedure. Twenty-four hours after the procedure, complete PDA occlusion was verified in 3 additional patients. One patient who underwent coil occlusion was discharged with minimal residual shunt and was lost for observation. Immediately after the occlusion the systolic-diastolic murmur on auscultation was absent in 12 patients. In 7 patients the murmur disappeared within the next 24 hours after the procedure. All patients were discharged within 3-4 days postprocedure. No complication occurred. Control examination and echocardiography were performed at 1, 3 and 6 months. Adequate anchorage of the coil and the occluding device was confirmed in all patients, no shunt through the PDA was revealed.

Absence of immediate left-to-right shunt at the level of atria following the implantation of Amplatzer septal occluder was confirmed in 3 out of 6 patients with ASD. Control echocardiography was performed also at 3, 12 and 24 hours postprocedure. Twelve hours after the procedure another 2 patients had no signs of shunt. There was one failed occluder implantation in a patient with large-sized ASD (38 mm). The device was withdrawn into the delivery system and removed from the heart. No complications were seen after device implantation. Three patients underwent control examination at 1, 3 and 6 months, and 2 patients - at 1 month after the procedure. Echocardiography confirmed the adequate positioning of the device and absolute absence of shunting in all 5 patients with the implanted Amplatzer device.

Discussion.

Various methods of transcatheter closure of abnormal communications between the systemic and pulmonary circulations have been applied for quite a long time. Endovascular closure of PDA depending on the type of occluding device has more than 30-year history, and T. King and N. Mills reported transcatheter closure of ASD as early as in 1976 [3,6,9]. In spite of successful applying of various endovascular occluding systems, the work at their improvement is carried out continuously. In our opinion the main benefits of detachable Flipper coils and self-centering devices Amplatzer Duct Occluder or Amplatzer Septal Occluder are the following: implantation simplicity and security, small diameter of delivery system, controllable implantation procedure and possibility to remove inadequately implanted device.

At the same time the application of various occluding devices has some special features. The diameter of coils used for PDA closure, depending on the technique, must be no less than twice as large as the pulmonary end of the duct. However, Flipper coils have limited application because of their diameter of 8 mm, therefore diameter of the duct must be at the most 4 mm. In our experience we faced two cases when the duct diameter was within 3.5 mm, but significant residual shunt was seen after single coil implantation. We attempted to implant additional coils placing the loops of the next coil in aortic infundibulum across the loops of already implanted coil. In our opinion, this approach determines optimal conditions for the accelerated thrombogenesis in case of well differentiated aortic infundiulum. However, we have to keep in mind that repeated PA trunk catheterization through the PDA requires particular precautions related to higher risk of the first coil dislocation into the pulmonary artery. In case of additional coils implantation, we adhered to the policy that delivery catheter should be placed in the aortic infundibulum and the duct should be catheterized by the coil itself, anchored within the delivery device, using the system "coil-delivery device" as a guide. Then the loops were formed at the pulmonary and aortal sites as described above. No cases of coil dislocation into PA were observed using this approach.

Published data regarding results of the use of Amplatzer Septal Occluder (ASO) systems [3,9,12]

seems very encouraging. The results of the first operations in our country performed at Bakoulev Scientific Centre for Cardiovascular Surgery also confirmed high efficacy of this method of heart defect correction. Fortunately, we had not any objective troubles in device implantation while performing the first procedures of transcatheter ASD closure, using ASO in our centre. Only one failed device implantation was related, in our opinion, to excessive thickness of superior septal rim in combination with the large-sized defect which was confirmed during open surgical closure performed in this patient two days later.

We met a certain inadequacy between the results of ASD size determination on the base of transthoracic echocardiography and with direct evaluation during balloon sizing. Such an inadequacy is determined by a certain "stretching" of the defect rim during ballooning due to its anatomic elasticity. We consider just this size to be the true one, because the "filling" effect is obtained during device implantation, so that residual shunting is minimized. The results of our procedures confirm the accuracy of such approach.

Conclusions.

1. Transcatheter occlusion is an effective method for radical treatment of PDA and ASD.

2. With proper patients selection and accuracy in procedure performing the rate of complications is minimal.

3. Minor operative trauma, good cosmetic effect, essential shortening of in-hospital stay (up to 3-4 days) are indisputable benefits of transcatheter closure of ASD and PDA as compared with traditional surgical correction.

4. Transthoracic echocardiography underestimates the size of atrial septal defect on average by 34.6%, and it must be kept in mind during patients selection.

References:

1. Freed M., Grines C. Cardiology tables and schemes. Moscow, Praktika publishers, 1996.

2. Belokon N.A., Podzolkov V.P. Congenital heart diseases. Moscow, 1991.

3. Bockeria L.A., Podzolkov V.P., Alekyan B.G. Endovascular and minimally invasive surgery of the heart and vessels in children. Bakoulev Scientific Center for Cardiovascular Surgery, Russian Academy of Medical Sciences, 1999

4. Bourakovsky V.I., Bockeria L.A. Cardiovascular Surgery. Moscow, 1996

5. Alekyan B.G., Podzolkov V.P., Garibyan V.A. et al. Catheter therapy of congenital cardiovascular diseases. Vestnik rentgenologii, 1996, 5, 10-21.

6. Alekyan B.G., Podzolkov V.P., Kardenas K.E. et al. Transcatheter embolization in the treatment of some congenital heart diseases. Grudnaya i Serdechno-Sosudistaya Khirurgia, 1996, 6, 226.

7. Alekyan B.G., Petrosyan Yu.S., Garibyan V.A. et al. Endovascular surgery in the treatment of congenital heart diseases. Annaly Khirurgii, 1996, 3, 54-63.

8. Alekyan B.G., Kardenas K.E., Mitina I.N., Plotnikova L.R. Transcatheter closure of the PDA using Gianturco coil. Grudnaya i Serdechno-Sosudistaya Khirurgia, 1997, 1, 20-24.

9. Alekyan B.G., Mashura I., Pursanov M.G. et al. Closure of atrial septal defects using "Amplatzer septal occluder" - first experience in Russia. International symposium "Minimally invasive surgery of the heart and vessels". Moscow, 1998, 23.

10. Bankl G. Congenital defects of the heart and large vessels. Moscow, Medizina publishers, 1980, 113-120.

11. Krichenko A., Benson L., Burrows P et al. Angiographic classification of the isolated persistenly patent ductus arteriosus and implications for percutaneous catheter occlusion. Am.J.Cardiol., 1989

12. Masura J., Gavora P., Formanek A., Hijazi Z. M. Thranscatheter closure of secundum atrial septal defects using the new self-centering Amplatzer septal occluder: initial human experience. Cathet. Cardiovasc. Diagn., 1997

13. Benson L. Catheter Closure of the ductus arteriosus In: Rao P.S. (ed).: Transcatheter Therapy in Pediatric Cardiology, New York, Wiley-Liss, 1995, 321-333.

14. Cook Cardiology Europe Brochure. Detachable coils for PDA closure, 1994.

15. Hijazi Z. V., Geggel R. L. Results of antegrade transcatheter closure of patent ductus arteriosus using single or multiple Gianturco coils. Am. J. Cardiol., 1994, 74, 925-929.

16. Kirklin J. W., Barrat-Boys B. G. Cardiac Surgery. New York, John Wiley, 1987, 945-955.

17. Rao P. S., Sideris E. Transcatheter occlusion of patent ductus arteriosus: Which method to use and which ductus to close? Am. Heart J. (In Press).

18. Rashkind W. J., Cuaso C. C. Transcatheter closure of a patent ductus arteriosus: Successful use in a 3,5 kg infant. Pediatr. Cardiol., 1979, 1, 3-7.

19. Sideris E. B., Leung M., Yoon J. H., Chen C. R., Lochan R. et. al. Occlusion of large atrial septal defects with a centering buttoned device. Am. Heart J., 1996, 131, 356-359.

20. Sideris E. B., Sideris S. E., Fowlkes J. P. et. al. Transvenous atrial septal defect occlusion in piglets. Circulation, 1988, 78, 11-99.

21. Hijazi Z. M., Marx G. R. Transcatheter closure septal defect and patent foramen ovale: Angel Wings. Frontiers in interventional Cardiology, Martin Dunitz LTD, 1997, 444-449.

22. Edmunds H. Cardiac Surgery in the Adult. New York, 1996

Causes of in-stent restenosis

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In-stent restenosis develops in 15% to 40% of patients after stenting procedure. Restenosis morphology is substantially different from that of restenosis following balloon angioplasty and has few common traits with atherosclerotic process. The underlying mechanism of restenosis can be explained by excessive intimal proliferation. As the therapeutic approaches to treat in-stent restenosis differ from those established for primary lesions, prediction of treatment-resistant types of restenosis makes a clinical challenge.

In 63% of cases the in-stent restenosis is found to be diffuse and exceeding 10 mm in length. In over half of cases the in-stent restenosis develops more aggressively than primary lesions. Diffuse and aggressive restenosis is more common in women, diabetic patients, after stenting for coronary occlusions or the use of wire stents and long stents.

Keywords: in-stent restenosis, diffuse restenosis, aggressive restenosis, predictors of restenosis.

Coronary stenting has substantially, though incompletely, reduced the rate of restenosis and the need for repeated percutaneous coronary interventions (PCI) as compared to balloon angioplasty alone. Investigators showed that balloon angioplasty is ineffective in some patients with in-stent restenosis (ISR) (1). It was demonstrated that percutaneous transluminal balloon angioplasty was successful in patients with centrally located in-stent restenosis; however, diffuse in-stent restenosis was more likely to recur after plain balloon angioplasty (2). This study revealed different patterns of diffuse and aggressive in-stent restenosis.

Materials and methods.

Patients with coronary artery disease were clinically assessed during 6 months following stenting performed during the period from 1998 to 2002. All patients who underwent stent implantation with uneventful recovery during the first 14 days were advised to visit their doctors at 4-6 months for clinical assessment. Among these, 502 patients underwent repeated catheter interventions for angina recurrence or other cardiac events. In-stent restenosis exceeding 50% of vessel lumen diameter was revealed by coronary angiography in 465 patients.

Previous studies performed by the International Research Group of Invasive Cardiology demonstrated the major correlations between the in-stent restenosis and longer stents, smaller lumen diameter of stented segment, type D, E and F dissection, elderly patients, prior history of coronary bypass grafting (3,4). These studies largely comply with the results reported by other authors (5-10).

Statistical analysis was performed with Statistica for Windows 6.0 application package (StatSoft Inc., USA, 2001). Sample distribution pattern was assessed. Single-factor variance analysis was used for primary comparison of values between groups with normal distribution. Values with significant rightward shifted distribution were generally analyzed using logarithmic scale. Values for each group were summarized in the tables as mean value ± standard deviation.

The correlation between in-stent restenosis and its predictors was assessed using logistic regression methods. Significant predictors revealed by single-factor regression analysis were included into a multifactor model. Step-by-step elimination of variables was performed in order to remove insignificant predictors. The results of single-factor and multifactor models were presented as odds ratios (OR) and 95% confidence interval (CI).

Results.

Diffuse changes were found in 63% of ISR patients, occlusions occurred in 18% of the total number of ISR. Differences between groups with diffuse and non-diffuse ISR are presented in Table 1 and the significant predictors of diffuse ISR are shown in Table 2. Diffuse restenosis was found to be associated with smaller target vessel diameter (TVD), smaller baseline minimal lumen diameter (MLD), longer lesion, smaller final MLD, diabetes mellitus and female sex. The use of wire stent also significantly correlated with ISR. Multifactor model showed that ISR significantly correlated with diabetes mellitus, longer lesion, smaller final minimal vessel diameter and the use of wire stents.

When restenosis was reported in the first types of stents, the prevalence of diffuse changes was over 50% and there was no difference between slotted tube and wire stents in the proportion of diffuse in-stent restenosis (53% in Wiktor wire stents vs 58% in Palmaz-Schatz stents). However, ever since stenting has been performed for lesions of various severity,

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Table 1. Values of diffuse and aggressive in-stent restenosis groups.

	Diffuse	Local	P	Aggressive	Non aggressive	P
Clinical values						
Age (years)	59±10	60±11	NS	60±10	59±11	NS
Sex (women)	13%	6%	0.01	12%	5%	0.03
Hypertension	44%	48%	NS	46%	47%	NS
Diabetes mellitus	9%	10%	NS	9%	11%	NS
Smoking	61%	62%	NS	60%	65%	NS
LVEF	59±11	58±11	NS	58±11	58±12	NS
Multi-vessel disease	68%	72%	NS	69%	72%	NS
Unstable angina	28%	32%	NS	31%	28%	NS
Angiographic values						
Baseline min. diameter (mm)	0.7±0.5	0.8±0.5	0.02	0.8±0.5	0.6±0.4	0.001
Lesion length (mm)	16±9	12±7	0.001	14±8	18±12	0.001
Target vessel diameter (mm)	2.9±0.5	3.0±0.6	0.007	2.9±0.5	3.0±0.5	NS
Stenosis of the artery's origin	9%	15%	NS	12%	8%	NS
Occlusion at baseline	21%	12%	0.02	15%	24%	0.04
Bifurcational lesion	33%	30%	NS	33%	26%	NS
Severe calcification	15%	17%	NS	16%	13%	NS
Visible thrombus	2%	1.4%	NS	2%	1%	NS
Final min. diameter (mm)	2.9±0.6	3.1±0.6	0.001	2.9±0.6	3.0±0.5	NS
Procedural values						
Number of stents per patient	2.2±1.5	1.9±1.4	NS	2.1±1.3	2.1±1.6	NS
Types of stents						
Slotted tube	73%	89%	0.001	77%	82%	0.01
Wire	27%	11%	0.001	23%	18%	0.01
Stent length (mm)	38±26	29±20	0.001	36±25	33±22	NS
Final balloon diameter (mm)	3.5±0.5	3.5±0.4	NS	3.5±0.5	3.5±0.4	NS
Balloon/artery ratio	1.23±0.19	1.20±0.20	NS	1.23±0.20	1.20±0.19	NS
Final pressure (atm)	15±4	16±4	NS	15±4	16±4	NS
Stenting for dissection	19%	13%	NS	18%	16%	NS
Additional stent placement for longer lesions	17%	14%	NS	17%	11%	NS

therefore, the rate of diffuse restenosis in wire stents became to increase substantially, reaching 91% for Gianturco-Roubin II stent.

Technical features associated with the achievement of larger stent lumen had no significant effect on diffuse ISR rate. Final diameter of the balloon used to expand the stent, the ratio between balloon diameter and target vessel diameter as well as the balloon inflation pressure had no significant influence on the development of diffuse ISR. Diffuse ISR was associated with smaller changes of lumen diameter during PCI as compared to local ISR. Sixty eight per cent of patients with diffuse ISR initially had multi-vessel disease and most of them received more than one stent. Similar to other studies, ISR found in one vessel segment was a risk factor for ISR in another vessel segment (54% vs 18% of single-vessel ISR). The risk of ISR in another vessel segment in patients with prior history of ISR was increased 5.3-fold (p<0.001). The risk of diffuse ISR was increased 3.5-fold (CI = 1.45-8.45, p<0.005) in patients with diffuse ISR in another coronary artery segment.

Aggressive restenosis was defined as: 1) an increase of lesion length, and/or 2) decrease of MLD caused by ISR compared to baseline MLD. Late loss of lumen diameter was higher in aggressive ISR group (2.2 ± 0.7 mm vs 1.9 ± 0.6 mm, p<0.001) despite smaller immediate increase of lumen diameter follow-

Table 2. Predictors of diffuse in-stent restenosis.

Predictors	Single-factor analysis			Multifactor analysis		
	OR	95% CI	p	OR	95% CI	p
Clinical						
Female sex	2.41	1.19-4.90	0.015	1.87	0.87-4.00	0.1
Diabetes mellitus	2.85	1.19-6.85	0.019	3.50	1.45-8.45	0.005
Angiographic						
Baseline MLD	0.61	0.40-0.91	0.02	0.83	0.47-1.48	0.5
Baseline TVD	0.59	0.40-0.87	0.008	0.78	0.45-1.34	0.4
Baseline occlusion	1.65	0.95-2.88	0.08			
Lesion length	2.16	1.52-2.98	0.0001	1.70	1.27-2.27	0.0004
Final MLD	0.46	0.32-0.65	0.0005	0.57	0.35-0.90	0.02
Procedural						
Stent length	1.09	0.95-1.26	0.20			
Wire stent	1.62	1.01-2.59	0.04	2.29	1.11-4.69	0.02

Table 3. Predictors of aggressive in-stent restenosis.

Predictors	Single-factor analysis			Multifactor analysis		
	OR	95% CI	p	OR	95% CI	p
Clinical						
Female sex	3.73	1.43-9.73	0.007	2.76	1.03-7.39	0.04
Diabetes mellitus	8.81	1.18-66.0	0.03	2.65	1.02-6.24	0.04
Angiographic						
Baseline MLD	2.74	1.81-4.15	0.001	5.13	2.57-10.2	0.001
Baseline occlusion	0.56	0.50-1.14	0.2			
Lesion length	0.52	0.44-0.63	0.001	0.68	0.50-0.91	0.004
Procedural						
Stent/lesion length	1.32	1.01-1.75	0.03	1.65	0.64-4.24	0.3
Wire stent	1.94	1.11-5.37	0.01	1.37	1.01-1.82	0.04

ing PCI (2.1 ± 0.7 mm vs 2.4 ± 0.6 mm, p<0.001). Differences between groups with aggressive and non-aggressive ISR are summarized in Table 1, and Table 3 shows significant predictors of aggressive ISR.

Aggressive in-stent restenosis was more common in women, patients with diabetes mellitus, in shorter lesions and greater baseline MLD. The use of wire stents and longer stents increased the risk of ISR as well. Occlusion wasn't found to be a statistically significant predictor of aggressive ISR. Multifactor analysis showed that female sex, diabetes mellitus, high MLD at baseline, short primary lesion and the use of wire stent were significant predictors of aggressive restenosis.

Statistically significant differences were found in the relationship between aggressive and diffuse restenoses: aggressive restenosis was significantly more common for diffuse lesions (57% vs 34%, p<0.001). Aggressive restenosis was the first event following PCI if the ISR was longer and more complicated compared to the primary lesion. If the aggressive restenosis was defined on the basis of a single criterion (longer or more complicated) then it occurred later. Non-aggressive ISR was the most delayed event following intervention (see Figure 1). Clinical signs were significantly more common in aggressive restenosis (47% vs 35%, p<0.05). Acute coronary syndrome (see Figure 2) was significantly more common for aggressive ISR with complicated and long lesion (6% vs 0.5% in non-aggressive ISR, p<0.02). Aggressive ISR with complicated lesion was more commonly associated with acute coronary syndrome as compared to aggressive ISR with long lesion (4.8% vs 2.1%, p<0.05).

Discussion

Previous studies performed by the International Research Group of Invasive Cardiology (3,4) and other investigators (5-8) revealed many ISR predictors. However, the degree and severity of in-stent restenosis played at least equal role as compared with the presence of ISR per se. Thus, ISR length was shown to be a significant predictor of recurrent restenosis following PCI for ISR (1). Prolonged ISR was more common if the primary lesion was long. However, highly complicated ISR could occur in short primary lesions as well (7).

Predictors of aggressive ISR were analyzed using a single-factor and multifactor logistic regression models. Large baseline MLD and short primary lesion revealed during angiography were significant predisposing factors for aggressive ISR as suggested by single-factor and multifactor analyses. Similarly, vessel with smaller narrowing of lumen following PCI were more prone to restenosis after PCI than vessels with subtotal occlusion or high-grade stenosis before inter-

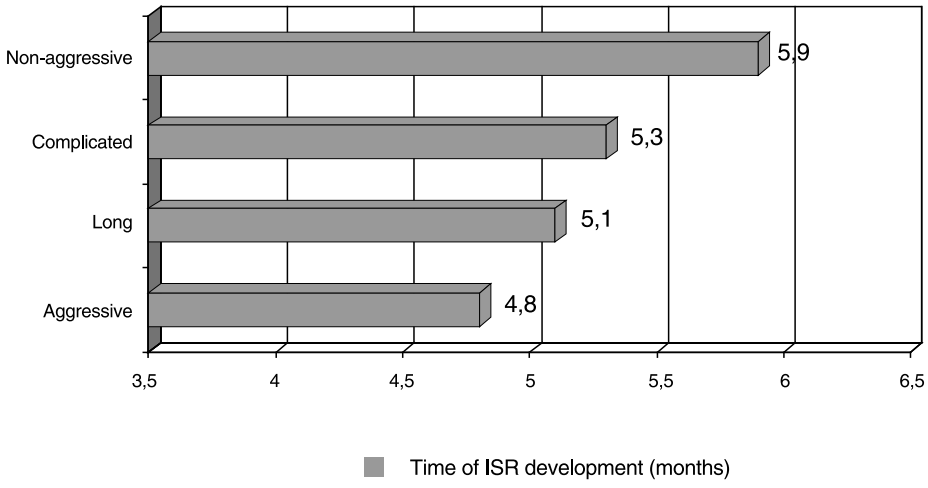

Figure 1. Correlation between type and time course of ISR

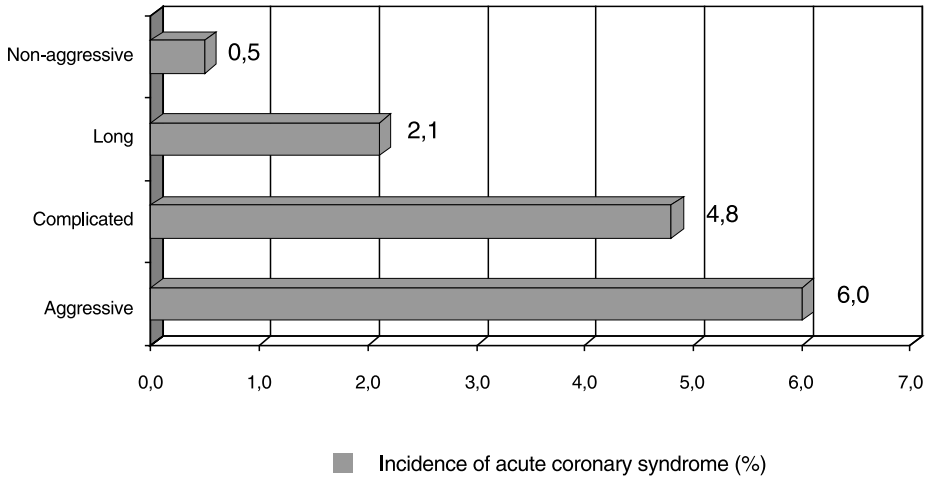

Figure 2. Correlation between ISR type and incidence of acute coronary syndrome.

vention.

Aggressive stenting with overdilatation and high inflation pressure are supposed to contribute to the development of aggressive ISR (5). However, our data are not sufficient to confirm this issue.

The correlation between large immediate increase of MLD and the development of aggressive restenosis seemed at first sight unusual. Instead of the current theory that restenosis is more common in smaller lumen (10), the study showed that successful immediate angiographic results following coronary artery stenting were more likely associated with aggressive ISR. Accordingly, lower immediate increase of MLD was less commonly associated with aggressive restenosis.

On the basis of previous studies, interventional cardiologists believe that wire stents have significantly higher rates of ISR. However, the ISR mechanism within these stents remains unclear. Published data concerning the role of stent type in the development of either aggressive or diffuse process are limited. We found, that the use of wire stent is a significant predictor of both diffuse and aggressive restenosis. An earlier study comparing Palmaz-Schatz and Gianturco-Roubin II stents demonstrated higher rate of ISR in Gianturco-Roubin II wire stent group and significant correlation between these stents and diffuse ISR.

Current study illustrated that the major variables predicting the presence or absence of restenosis, also have a role in the prediction of restenosis severity. Goldberg et al. assessed the role of final cross-sectional lumen area in ISR development (9). It appeared that restenosis should not be regarded as a dichotomous variable with insignificant (below 50% stenosis) and significant (above 50% stenosis) lesions. The tendency to consider ISR as a strictly dichotomous variable can possibly be attributed to marked clinical differences between these two conditions. This conventional theory, however, neither explains the difference between restenosis types, nor predicts the outcome. Whereas two stents can exhibit similar rates of ISR, the incidence of diffuse and aggressive IST may substantially differ. Yet, the difference between restenosis types following various stent implantation hasn't been reported. Such studies will possibly be performed with drug-eluting stents (covered with sirolimus, paclitaxel, everolimus).

Conclusion

Therefore, the in-stent restenosis is a major clinical problem. The number of patients with in-stent restenosis increases yearly due to more frequent stenting procedures. Significant proportion of restenotic lesions is presented by diffuse and aggressive lesions. Marked difference between in-stent restenosis and atherosclerosis require novel approaches to prevention and therapy.

References

1. Eltchaninoff H., Koning R., Tron C. et al. Balloon angioplasty for the treatment of coronary in-stent restenosis: immediate results and 6-months angiographic recurrent restenosis rate. J. Am. Coll. Cardiol., 1998,32,980-4.

2. Mintz G.S., Mehran R., Waksman R. et al. Treatment of in-stent restenosis. Semin. Interv. Cardiol., 1998,3,117-21.

3. I.V. Pershukov, Z.A. Niyazova-Karben, T.A. Batyraliev et al. Efficacy of excimer laser coronary angioplasty for the treatment of patients with restenoses after coronary artery stenting. Kardiologia, 2003,10,35-44.

4. Pershukov I., Niyazova-Karben Z., Batyraliev T. et al. Predictors of early in-stent restenosis. Am.J.Cardiol., 2003,92,6, Suppl.1, 207-208L.

5. Kornowski R., Hong M.K., Tio F.O. et al. In-stent restenosis: contributions of inflammatory responses and arterial injury to neointimal hyperplasia. J. Am. Coll. Cardiol., 1998,31,224-30.

6. Mehran R., Dangas G., Abizaid A. et al. Angiographic patterns of in-stent restenosis: classification and implications for long-term outcome. Circulation, 1999,100,1872-8.

7. Mehran R., Mintz G.S., Pichard A.D. et al. Morphologic and procedural predictors of diffuse in-stent restenosis. J. Am. Coll. Cardiol., 1997,29,76A.

8. Mercado N., Boersma E., Wijns W. et al. Clinical and quantitative coronary angiographic predictors of coronary restenosis. J. Am. Coll. Cardiol., 2001,38,645-52.

9. Goldberg S.L., Loussarian A., De Gregorio J. et al. Predictors of diffuse and aggressive intrastent restenosis. J. Am. Coll. Cardiol., 2001,37,1019-25.
10. Kuntz R.E., Safian R.D., Carrozza J.P. et al. The importance of acute luminal diameter in determining restenosis after coronary atherectomy or stenting. Circulation, 1992,86,1827-35.

Immediate and mid-term angiographic outcome of coronary stenting with BX stents (Sonic and Velocity) (Cordis, Johnson & Johnson) in patients with CHD. A single-center study.

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List of abbreviations.

LAD - left anterior descending artery
CA - circumflex artery
(a branch of the left coronary artery)
RCA - right coronary artery
DA - diagonal artery
MA - marginal artery of CA or RCA
EP - endovascular procedure
AMI - acute myocardial infarction
LVEF - left ventricular ejection fraction.

Interventional cardioangiology is one of the most thriving trends of modern invasive medicine. Procedural and technical innovation, which have replenished this field of medical practice, enlarge the potential of cardiology making real what once had been an unrealizable dream. Less than twenty years have passed since the day, when a self-expanding nitinole coronary stent was first implanted by Jacques Puel (Toulouse, France) (1), followed by the manufacturing and clinical use of intracoronary stents (Gianturco-Roubin, Palmaz-Schatz, and, more recently, Multi-Link, AVE GFX, NIR and etc). Already the first studies demonstrated the benefits of stenting over balloon angioplasty as regards to immediate and long-term clinical-and-angiographic outcome (2, 3), thus favoring the search for novel technical solutions and the development of coronary stenting. Over 50 types of coronary stents have been introduced by the manufacturers for the past few years.

Stenting of coronary arteries and other arteries carrying blood to vital organs has been performed in the Center since 1997. Currently we have an experience of several thousands stenting procedures with various stent types. This article summarizes our own experience with matrix coronary stents of BX family, which were implanted in a single facility by practically the same team of physicians, therefore increasing homogeneity of the results due to the universal tactics and methods of patient selection, technical features of the endovascular procedure, and further medical therapy.

As a part of the research schedule, all patients with endovascular coronary procedure performed in the Center of Interventional Cardioangiology (Moscow) were advised to undergo repeated examination (including coronary angiography) 6 months following the invasive procedure. Therefore, we have gained an experience, which ensures reliable assessment of immediate and long-term outcome with various types of coronary stents.

Purpose of the study was to evaluate the immediate and mid-term results of coronary artery stenting with BX matrix stents of similar design: BX Sonic and BX Velocity (Cordis, Johnson & Johnson, USA). The BX stents are made from a solid tube with an appropriate diameter (316L medical steel) by laser treatment with subsequent electronic polishing. Both stents have a closed-loop mesh (see Figure 1) and different delivery systems: Raptor balloon catheter for BX Velocity stent and U-Pass system for BX Sonic stent. The range of length and diameter is also similar: 2.25, 2.5, 2.75, 3.0, 3.5, and 4.0 mm diameter (excluding the BX Velocity stent with maximum diameter of 5 mm); length ranges from 8 to 33 mm (with 5 mm increment). The nominal diameter is achieved by the inflation of delivery balloon at 10-12 atmospheres (burst pressure 16 atmospheres). Distal end of the stent delivery system is 2.7 Fr in diameter.

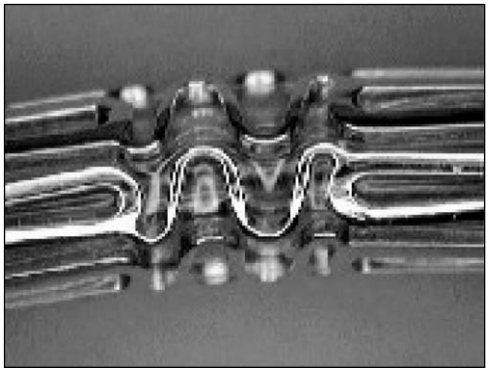

Figure 1.

Patient clinical description.

A total of 584 BX stents were implanted between January 2001 and October 2004 in Moscow Research and Practice Center of Interventional Cardioangiology

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(112 BX Velocity stents vs 472 BX Sonic stents) in 526 native coronary arteries of 491 patients for primary (de novo) atherosclerotic stenosis. Apart of the above BX stents, 87 stents of other types and manufacturers were used in 86 arteries of 71 patients (14.5%). Table 1 shows the clinical manifestations and medical history of the patients studied. The mean age was 58±12.4 years (range 32 to 83 years), the vast majority of patients were men - 401 (81.7%). Angina of effort with different NYHA functional class was the cause for examination and treatment in most patients - 306 (62.3%); unstable angina was found in 121 (24.6%) patients; acute myocardial infarction - in another 64 patients (13%), of these: 38 patients underwent the endovascular procedure within 6 hours following the onset of AMI vs 14 days in the remaining 26 patients.

Table 1. Clinical manifestations and medical history of study group patients (n=491)

Parameter	Number
Mean age	58±12.4 years
Male patients	401 (81.7%)
Diagnosis:	
NYHA 2-4 class angina of effort	306 (62.3%)
Unstable angina	121 (24.6%)
Acute MI	64 (13%)
Diabetes mellitus	59 (12%)
History of MI	187 (38.1%)
LVEF≤40%	61 (12.4%)

Selective coronary angiography and endovascular procedures were performed according to standard technique with Cordis (USA) diagnostic catheters and guidewires. Quantitative analysis of angiographic images was performed by Hicor computer of Coroscop Classic angiography unit (Siemens, Germany). Pooled angiographic data are summarized in Table 2.

Table 2. Results of selective coronary angiography and left ventricular angiography of the groups studied.

Parameter	Number
≥2 arteries involved	161 (32.8%)
Target lesion location:	
LAD	307 (52.6%)
CA	76 (13%)
RCA	162 (27.7%)
DA/MA	39 (6.7%)
Mean reference diameter at the site of EP (mm)	2.97±0.52
Mean stenosis degree (%)	81±16.7
Mean stenosis diameter prior to the procedure (mm)	0.71±0.31
Mean vessel diameter following the procedure (mm)	3.02±0.32
Primary stenosis type B2/C	384 (65.8%)
Chronic occlusion	63 (10.8%)
Acute occlusion	34 (5.8%)
Mean stenosis length (mm)	13.8±6.1

With preserved minimum artery lumen and TIMI 2-3 antegrade flow direct stenting was attempted. Stenting was performed at the nominal or higher pressure according to compliance table so as to achieve the desired stent diameter and avoid residual stenosis. Success was defined as: residual stenosis ≤30% from the target portion reference diameter; TIMI3 antegrade flow; absence of threatened dissection or occlusion of major side branches. Uneventful recovery was defined as the absence of AMI recurrence, major rhythm disorders, clinical signs of heart failure, puncture site disorders and other complications (bleeding necessitating blood transfusion or surgery), need for repeated revascularization.

Follow-up study (including selective coronary angiography and left ventricular angiography) was performed in 281 (57.2%) patients 7.8±2.4 months following stenting. Long-term results assessment was based on the following endpoints: mortality rate, acute myocardial infarction, angina recurrence, repeated revascularization procedure of the target artery). A total of 324 stents were assessed angiographically (62 BX Velocity stents vs 262 BX Sonic stents). Restenosis was defined as a reduction of lumen diameter within the stent (in-stent stenosis) or in the adjacent segments (in-segment stenosis) ≥50% from the reference diameter. Occlusion of the treated segment was identified by the absence of distal antegrade flow (TIMI 0).

The following methods of statistical analysis were used to assess the difference between follow-up and baseline characteristics: Spirmen rank correlation coefficient, Mann-Whitney test (non-parametric criterion for the contrast of means), and Wilkokson (non-parametric paired test for the contrast of means).

Results and discussion.

Immediate angiographic success was achieved in 577 of 584 stent implantation procedures (98.8%). This complies with the results of VENUS multicenter study dedicated to the use of BX Velocity stents, suggesting 96.7% efficacy of the procedure. Similar results were reported by A. Kastrati et al., who compared five types of stents (4). An optimal outcome was not achieved in the remaining 1.2% of patients due to threatening flow-limiting circulatory dissection at the distal end of the stent - in 3 patients; lateral branch occlusion causing AMI with failure to restore blood flow - in 2 patients; no-reflow effect - in another 2 patients (in both cases the intervention was performed for acute occlusion of the infarction-related coronary artery). Of the 423 attempts of direct stenting 411 were successful (97.2%). Of the 12 failures to advance the stent through the lesion without predilation 5 were with BX Velocity stents (41.6%), and 7 - with BX Sonic stents (48.4%). High per cent of successful direct stenting emphasizes the high "permeability" of low-profile stent delivery complexes and complies with the results of Serruys P. et al. (5), who assessed the outcome of direct stenting. High "per-

meability" of BX stents was reported as well by Wei-Chin Hung et al., who analyzed the results of direct stenting in internal thoracic artery bypass (6). We believe, that the low-profile design provides optimal visualization, ensuring successful positioning and clear visualization of the stent during follow-up examination on one hand, and convenient assessment of stent lumen and blood flow by the physician on the other hand. No cases of stent dislocation or delivery balloon burst were observed, thus making the results well predictable as regards to technicality. Clinical and angiographic results of hospital follow-up are shown in Table 3.

Three patients (0.6%) died during hospital stay. In one patient the death was due to Q-wave AMI causing progressive myocardial dysfunction despite the successful flow restoration in the LAD within the first 6 hours after the disease. Two other patients (0.4%) died due to stent thrombosis within the first hours following the procedure causing cardiogenic shock resistant to medical therapy in patients with severe myocardial dysfunction (LVEF≤40%) and three-vessel coronary disease.

Table 3. Immediate angiographic and clinical results of stenting procedures in both groups studied.

Parameter	Number
Angiographic success	577 (98.8%)
Artery lumen diameter after stenting (mm)	302±0.32
Uneventful recovery	469(95.5%)
Complications:	
AMI/Q-wave	4(0.8%)/2(0.4%)
Hospital mortality rate	3(0.6%)
Repeated EP	9(1.8%)
Vascular complications	6(1.2%)
Acute psychosis	1(0.2%)

Serious adverse events occurring at the site of puncture (1.2%) included retroperitoneal or subcutaneous hematoma necessitating blood transfusion in one patient; pulsative hematoma in another 4 patients (surgery was attempted in a single case, in the remaining 3 patients hematoma was removed by repeated pressure at the puncture site). Acute thrombosis of femoral artery was observed in one patient and removed by means of surgery.

Mean hospital stay in the total patient population was 2.8 days following the procedure vs 8.6 days in AMI group (p<0.05). In patients with angina this value was 8.1 days. Uneventful recovery was observed in 95.5% of patients during hospital stay.

Control examination, as indicated above, was performed in 281 (57.2%) patients, extrapolating 57.2% of all patients with stents, enrolled in the study. Angiographic assessment included 324 stents (62 BX Velocity and 262 BX Sonic). Table 4 shows the results of follow-up selective coronary angiography.

Results of the mid-term follow-up coronary angiography performed in the total patient population suggest the 36.1% rate of in-stent and in-segment (+5 mm) restenosis and 2.5% rate of stent occlusion. These data comply with the above mentioned VENUS study, which suggested 33.8% rate of in-stent restenosis.

Table 4. Results of the long-term follow-up coronary angiography in the groups studied (n=281).

Parameter	Number
In-segment restenosis	117 (36.1%)
In-stent restenosis	104 (32.1%)
Diffuse restenosis	62 (19.1%)
Local restenosis	42 (12.96%)
Stent occlusion	8 (2.5%)

Correlation analysis (Spearmen rank correlation test) was performed to reveal baseline factors of clinical manifestations, medical history and angiographic findings affecting the course of the disease as a whole and, in particular, on the condition of stent and the treated vessel. We found significant correlation between the unfavorable outcome of stenting (restenosis or occlusion) and vessel lumen diameter immediately after the stent implantation less than 3.0 mm in diameter (R=-0.302; p<0.03); the site of stent placement (namely the origin and the proximal portion of LAD (R=0.280; p<0.04); complicated lesion morphology at baseline (C-type lesion) (R=0.270; p<0.04). In addition, we found a trend towards the correlation between the restenosis and stent length over 13 mm (R=0.245; p<0.072). However, there was no significant correlation between the unfavorable long-term angiographic outcome and the clinical form of CHD, diabetes mellitus, hypertension, middle age, gender, smoking, dislipoproteinemia.

Correlation analysis revealed two groups of stents. The first group ("high risk" group) included stents (n = 111), implanted into the origin and the proximal portion of LAD due to complicated plaque morphology at baseline (type C lesion) and stents with lumen diameter ≤3.0 mm after the procedure (according to the results of computed quantitative analysis). In contrast, the second group was composed of stents (n = 46) implanted into RCA, CA and middle portion of LAD due to type A-B1 lesion and stents with lumen diameter >3 mm after the procedure. All other clinical data and medical history data were comparable between the groups. The analysis showed, that the rate of undesirable mid-term angiographic outcome (restenosis of occlusion) in the first group ("high risk" group) was 51.4%, whereas in the second group this value was 8.6% (p<0.002)!

Conclusion

The use of BX Velocity and BX Sonic matrix stents (Cordis, USA) ensures optimal immediate angiographic outcome in the vast majority of patients (98.8%). At the same time, weighted and individual approach to the choice of BX stents for morphologically complicated lesions (including baseline occlusions), particularly

for lesions located in the origin or proximal portion of LAD with <3 mm lumen diameter, provides significant reduction of the unfavorable long-term results, thus improving treatment quality and disease prognosis.

References:

1. Puel J., Joffre F., Rousseau H. et al. Endoprostheses coronariennes autoexpansives dans le prevention des restenoses apres angioplastie transluminale. Arch.Mal. Coeur, 1987, 8, 1311-1312.
2. Serruys P.W., De Jaegere P.P.T., Kiemeneij F. et al. Comparison of Balloon-expandable stent implantation with balloon angioplasty in patients with coronary artery disease. N. Engl. J. Med., 1994, 331, 489-495.
3. Macaya C., Serruys P.W., Ruygrok P. et al. Continued benefit of coronary stenting versus balloon angioplasty: One-year clinical follow-up of BeneStent Trial. In: "8-th complex coronary angioplasty course", Paris, May 20-23, 1997, 783-791.
4. Kastrati A., Dirschinger J., Boekstegers P. et al. Influens of stent design on 1 year outcome after coronary stent placement: A randomized comparison of five stent types in 1147 unselected patients. Cath. Cardiovasc. Interv., 2000, July, 50(3), 290-297.
5. Serruys P.W; Isselmuiden S. Hout B. Direct stenting with the Bx VELOCITY balloon-expandable stent mounted on the Raptor rapid exchange delivery system versus predilatation in a European randomized Trial: the VELVET trial. Int. J. Cardiovasc. Intervent., 2003, 5(1),17-26
6. Wei-Chin Hung, Bih-Fang Guo, Chiung-Je Wu et al. Direct stenting of transradial left inyernal mammary artery graft. Chag. Gung. Med. J., 2003, 26, 925-929.
7. George C.J., Baim D.S., Brinker A.J. et al. One-year follow-up of the Stent Restenosis study (STRESS I). Am. J. Cardiol., 1998, 81,860-865.
8. Lefevre T., Aimouch N., Louvard Y. et al. Stenting of Bifurcation Lesions Using the BX Velocity Stent: A Pilot Stady. Am. J. Cardiol., 2000, 86, 110i.

Regression of coronary artery lesions triggered by electric pacing.

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Objective.

To evaluate the effect of electrical pacing on human coronary atherosclerotic disease.

Background: It has been previously shown that using low-voltage electrical stimulation (ES) adjacent to the rabbit abdominal aorta led to reduction of localized atheroma. However, there're no data available regarding its effect on human coronary atherosclerotic disease.

Method.

We identified 19 patients who had undergone cardiac catheterization prior to pacemaker implantation and subsequently had repeat cardiac catheterization. Nineteen patients, matched for cardiac risk factors and medications, who underwent cardiac catheterization at least twice during the same time period served as controls. Coronary lesions that were ≥30% in severity on initial angiogram by quantitative coronary angiography (QCA) were analyzed. QCA was then repeated to compare the same lesions and any other new lesions at the follow-up angiograms.

Result.

A total of 107 lesions (61 lesions in the pacemaker group and 46 lesions in the control group) were identified. Over a period of 34 and 35 months follow-up respectively, there was a significant lesion regression of 13.26% in the pacemaker group and lesion progression of 13.21% in the control group. No new lesions were found in the pacemaker group. However, 24 new lesions were identified in the control group. Major adverse cardiac events and the need for revascularization were significantly higher in the control group.

Conclusion.

Our study demonstrates that low-voltage ES not only resulted in regression of coronary atherosclerotic lesions but also significantly lowered the serious consequences of coronary artery disease. This intriguing observation deserves further exploration.

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Abbreviations.

QCA: qualitative coronary angiography
ES: electrical stimulation
HMG-CoA Reductase Inhibitor:
3-Hydroxyl-3-methyl-Glutaryl
Coenzyme A Reductase Inhibitor
VEGF: Vascular endothelial growth factor
LDL: Low density lipoprotein
IVUS: Intra-vascular ultrasound
SD: Standard deviation
LAD: Left anterior descending artery
RCA: Right coronary artery

Introduction.

Despite current advancement in the treatment of coronary atherosclerotic disease, it remains the number one cause of death in developed countries (1). Endovascular and surgical revascularization provide temporary benefit to a focal lesion but do not address the underlying pathology of the atherosclerotic process. Lipid lowering therapy with HMG-CoA Reductase Inhibitors (statins) has been demonstrated to decrease cardiovascular morbidity and mortality through inhibition of de novo cholesterol synthesis (2). In addition, other studies (3-5) support the notion that statin therapy can stabilize plaque lesions by reducing their lipid content and inflammation. Furthermore, high-dose statin therapy has shown to cause significant regression of an established atherosclerotic lesion in human carotid and aortic arteries (6-7). However, its effect on human coronary atherosclerotic disease is under investigation at this time.

The safety and efficacy records of using low-voltage (≤5 volts) ES emitted from an implanted permanent pacemaker to treat brady-arrhythmia disorders has been proven over the years. Multiple studies using animal models suggest that ES has both beneficial and detrimental effects on the vasculature. Breuer et al (8) showed that high-voltage (≥9 volts) ES induced coronary artery plaque formation in a baboon model. Furthermore, Betz E. et al (9) demonstrated that high-voltage ES caused intimal hyperplasia of the carotid vessel in rabbits. To the contrary, low-voltage ES seem to have a beneficial effect on the vascular structure. Our previous experiments (10-12) using electric impulses with low-voltage ES adjacent to the rabbit abdominal aorta showed a significant decrease in atherogenesis. Multiple studies have also shown that low-voltage ES leads to increase

vascular endothelial growth factor production and angiogenesis. Hudlicka et al (13) demonstrated that low-voltage ES in cardiac bio-assist leads to doubling of capillary density in the target muscle fibers. Furthermore, chronic electrical stimulation of a latissimus dorsi cardiomyoplasty at 1.25Hz leads to significant latissimus-derived collateral bloods flow to the myocardium. However, there are no studies done to evaluate whether electrical pacing has any effect on coronary plaque except for a report by Mosseri et al (14) on coronary angiographic characteristic of patients with permanent artificial pacemakers. The objective of this study is to use QCA to evaluate the long-term affect of low-voltage ES from an implanted pacemaker on de novo coronary atherosclerotic lesions in humans.

Method.

Of the 946 patients who underwent permanent pacemaker implantation during the period of January 1994 to December 2002, 298 patients underwent cardiac catheterization prior to pacemaker implantation. Of these, 26 patients had a repeated cardiac catheterization after pacemaker implantation. Seven patients were excluded from the study because three patients had a normal coronary anatomy and four patients have a prior history of coronary artery by-pass surgery. Of the remaining 19 patients, coronary lesions that measured ≥30% in severity on initial angiogram by QCA (Sanders data, San Jose, CA) were analyzed. QCA was then repeated on the same lesions at the follow-up angiograms. Additionally, we also searched for any new lesions that measured ≥30% in severity on the repeat coronary angiograms. Nineteen patients who did not have pacemaker implantation, but underwent cardiac catheterization at least twice during the same time period, were matched for cardiac risk factors and medications as shown on Table 2 and used as controls. For quality assurance, two different investigators were independently performing QCA on all lesions. The degree of stenosis of each lesion is the average value derived from the two investigators. Pacemaker parameters of the pacemaker group are shown in Table I.

Statistical Analysis.

Data are presented as mean ± 1 SD. Statistical analysis was performed with chi-square for categorical data. The paired T-test was used for change with-in the two groups, and continued data T-test was used to analyze between pacer and control age-lesions.

Table 1. Pacemaker parameters.

Parameters	Results
Single/Dual-chamber pacing	2/17
Demanded/Permanent pacing	11/8
Range of atrium and ventricle voltage (Volt)	2.5-4/2.5-5
Average Range of pacing (%)	50-100

Data are presented as the number (%) of subjects.

Results.

Data regarding various clinical variables between the two groups at baseline (all non-significant) are listed in Table 2. During the initial coronary angiograms, a total of 61 lesions were identified in the pacer group and 46 lesions in the control group. There was significant coronary lesion regression (-13.26%) in the pacemaker group and lesion progression (+13.21%) in the control group after a mean follow-up period of 34.6 ± 22.1 and 35.6 ± 23.5 months respectively (Table 3, Figure 1). Furthermore, the repeat coronary angiograms did not identify any new lesions (≥30%) stenosis in the pacemaker group. However, there were 24 new lesions (≥30%) stenosis found in the control group. When each coronary artery was analyzed separately, all three vessels had a similar degree of lesion regression in response to low-voltage ES as shown in Figure 2. Lesions were further divided into those that have repeated coronary angiogram done within one year, 1-2 years, and more than two years. There was no further significant plaque regression noted after one year of pacemaker implantation (Figure 3).

Table 2. Demographic characteristics.

Variables	Pacer Group	Control Group	P Value
Age (year)	73.68 ± 8.49	68.0 ± 10.67	NS
Diabetes Mellitus	7 (36.8%)	9 (47.4%)	NS
Hypertension	8 (42.1%)	7 (36.8%)	NS
Hypercholesterolemia	8 (42.1%)	7 (36.8%)	NS
Smoking	6 (31.6%)	6 (31.6%)	NS
ACE inhibitor	13 (68.4%)	12 (63.2%)	NS
Beta-blocker	10 (52.6%)	6 (31.6%)	NS
Aspirin	10 (42.6%)	15 (78.9%)	NS
HMG-Coa reductase inhibitor	6 (31.6%)	6 (31.6%)	NS

Data are presented as the number (%) of subjects.
NS = no significant difference; ACE = angiotensin coverting enzyme; HMG-Coa = hydroxyl-methyl-glutaryl coenzyme A

Table 3. Angiographic Characteristics.

Variables	Pacer Group	Control Group	P Value
Duration of follow-up in months (range)	34.6 ± 22.1 (5-75)	35.6 ± 23.5 (8-92)	NS
Numbers of lesions at baseline	61	46	
Numbers of new lesions at follow-up	0	24	
Mean stenosis at baseline	41.79 ± 11.2%	33.90 ± 10.20	0.03
Mean stenosis at follow-up	28.53 ± 7.05%	47.11 ± 17.18	0.0001

Angiographic results of the initial and follow-up coronary angiograms.

Clinical follow-up of both groups showed that there was a significant reduction in major cardiac events

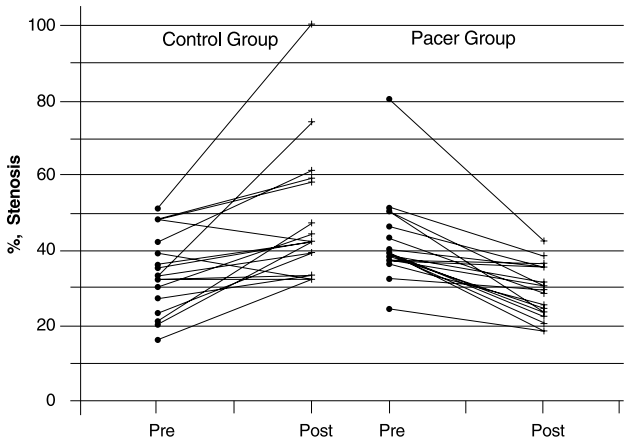

Figure 1. Mean coronary artery stenosis during the initial and follow-up angiograms.
Data are presented as mean coronary stenosis of each subject

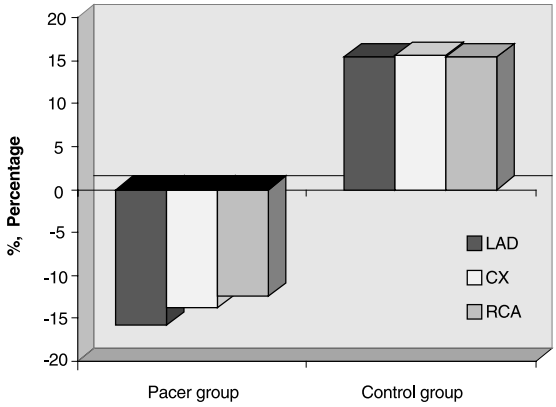

Figure 2. Mean percentage of lesion change in each coronary arteries.
Data are presented as the mean value.
LAD = left anterior descending artery;
CX = circumflex artery;
RCA = right coronary artery.

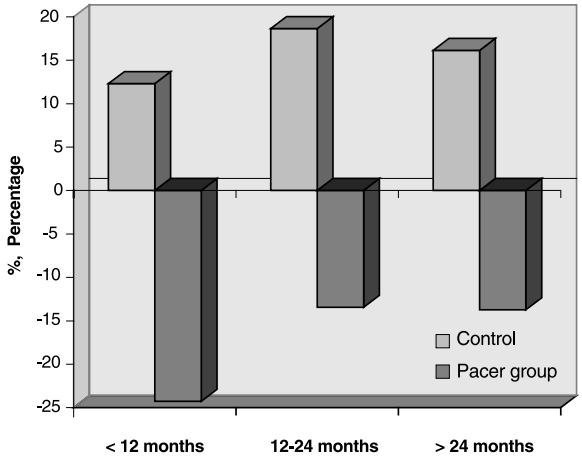

Figure 3. Mean coronary lesions change over times.
Data are presented as the mean value.

(unstable angina, myocardial infarction, and the need for revascularization) in the pacemaker group as compared to the control group [(2 vs. 9) p=0.02]. The two major cardiac events in the pacemaker group occurred at two and six months after the pacemaker implantation. One of these patients has a single chamber (right ventricle) pacemaker whereas the

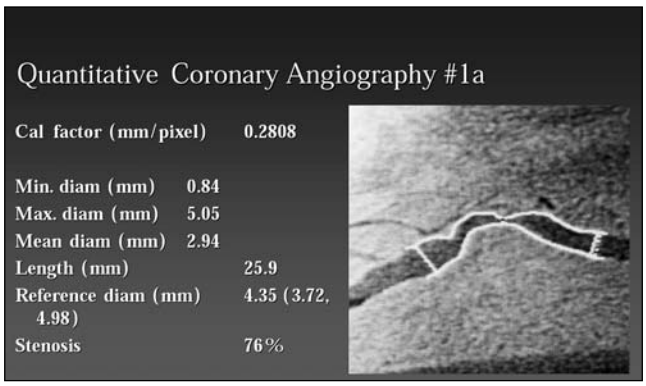

Figure 4.

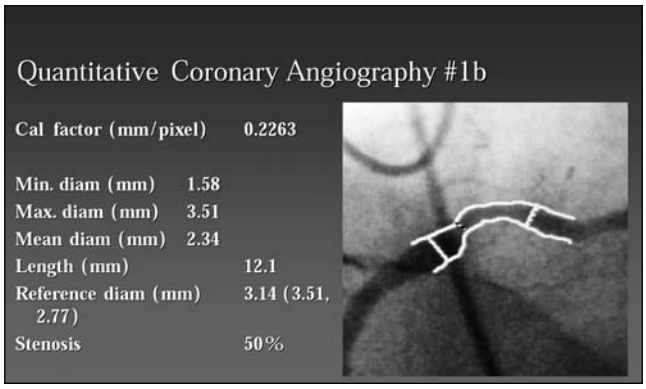

Figure 5.

other has a demanded dual-chamber pacemaker that paced at an average of 50%. Examples of QCA are presented in figures 4 and 5

Discussion.

In contrast to the detrimental effect of high-voltage ES (≥9 volts) on vascular structures as reported by Breuer et al (8) and Betz (9), our study suggests that low-voltage ES emitted by an implanted permanent pacemaker is not only safe, but also leads to significant coronary plaque regression and prevention of a new atheroma formation. Additionally, low-voltage ES seems to have a protective effect on the heart against major cardiac events such as unstable angina, myocardial infarction, and the need for revascularization. Given that the two major cardiac events in the pacemaker group occurred in a patient who has a single-chamber pacemaker, and a patient whose demand dual-chamber pacemaker only paced at an average of 50%, one can extrapolate that a dual-chamber pacemaker that paces at a rate of >50% would have better protective effect against major cardiac events. Our previous animal study (2) also suggested that the most effective pacing regimen against atherogenesis is with 100% pacing at an output of three volts. The effect of low-voltage ES on coronary atherosclerotic disease seems to be independent of any other known pharmacological intervention since there were no significant different in the cardiac risk factors and medications between the two groups (Table 2).

Our interest in evaluating the effect of ES on atherosclerosis came from previous studies where applying low-voltage ES to patients with cardiac

bioassist devices led to doubling capillary density in the target muscle fibers (13). Furthermore, the skeletal muscle then builds fatigue resistance by changing its phenotype from glycolytic to oxidative (17). The increase in vascularization is most likely due to the influence of ES on the morphology of the endothelial cells and on vascular endothelial growth factor (VEGF). It is well known that VEGF is a prototypic angiogenic growth factor that is associated with angiogenesis in vivo and causes endothelial cell proliferation in vitro (18,19). Annex et al. (20) strongly supported the hypothesis that some regimen of ES may play a positive role in severely ischemic tissue, showing that chronic motor nerve stimulation increases VEGF at the protein level. Hang et al. (21) showed similar findings by increasing VEGF protein in hypoxic muscle, especially in conjunction with ES. In addition, our previous works on the rabbit model also showed that low-voltage ES adjacent to the rabbit abdominal aorta led to significant inhibition of atherosclerotic plaque formation.

This study also supports our previous works in the rabbits showing that low-voltage ES inhibits atherosclerotic plaque formation. Furthermore, it seems to induce significant regression of coronary atherosclerotic lesions in human. The exact mechanism of how low-voltage ES induces retardation and regression of atherosclerotic plaque is unknown. However, one of the possible explanations is that low-voltage ES changes the distribution of iron in the vessel wall which leads to less redox-active iron to initiate lipid peroxidation, an important early event in the development of atherogenesis (22). In an animal model of atherosclerosis, (24) it was shown that the progression of atherosclerosis and low density lipoprotein oxidation are closely related to vascular iron deposition.

The morbidity and mortality of patients with permanent pacemaker implantation have been evaluated extensively in the past. A sub-analysis of a longitudinal follow-up of 1431 pacemaker patients by Jelic et al (15) showed that death due to coronary heart disease decreased after pacemaker implantation. Similarly, over a five-year follow-up period, Mattioli et al (16) reported that death contributed to myocardial infarction occurred in only 4.7% of 2243 pacemaker patients despite 560 of the patients having coronary artery disease prior to pacemaker implantation. Our study also confirmed that major adverse cardiac events were significantly lower in the pacemaker group. This is most likely due to the coronary atherosclerotic plaque regression. The other possible explanation is that there is more microvascularization in the capillary level secondary to the increase of VEGF induced by low-voltage ES as documented earlier by other investigators.

In this study, we only evaluated the effect of low-voltage ES on de novo coronary atheroma. The beneficial effect of low-voltage ES on de novo coronary atheroma may not be applicable to lesions in the vein graft or in-stent restenosis because of their different underlying pathogenesis. In fact, high-voltage ES has shown to induce intimal hyperplasia in the animal model. Therefore, further study is needed to evaluate the effect of low-voltage ES emitted by an implanted pacemaker on vein grafts and native coronary lesions that have been intervened. This is a retrospective study involving a small number of patients. To verify whether low-voltage ES truly has a beneficial effect of coronary atherogenesis, a large randomized prospective study with a more contemporary diagnostic device such as intravascular ultrasound (IVUS) will need to be done.

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References

1. Murray C.Y.L., Lopes A.D. The global burden of disease. Boston, MA, Harward School of Public Health/Harvard University Press, 1996, 1-34.

2. Corti R., Fuster V., Fayad Z. et al. Lipid lowering by simvastatin induces regression of human atherosclerotic lesions. Circulation, 2002, 106, 2884-7.

3. Aikawa M., Rabkin E., Sugiyama S. et al. An HMG-CoA Reductase Inhibitor, Cerivastatin, suppresses growth of macrophages expressing matrix metalloproteinases and tissue factor in vivo and in vitro. Circulation, 2001, 103, 276-283.

4. Crisby M., Nordin-Fredriksson G., Shah P.K. et al. Pravastatin treatment increases collagen content and decreases lipid content, inflammation, metalloproteinase, and cell death in human carotid plaques: implications for plaque stabilization. Circulation, 2001, 03, 926-933.

5. Zhao X.Q., Yuan C., Hatsukami T.S. et al. Effects of prolonged intensive lipid-lowering therapy on the characteristics of carotid atherosclerotic plaques in vivo by MRI: a case control study. Arterioscler. Thromb, Vasc. Biol., 2001, 21, 1623-29.

6. De Valk B., Marx M. Iron, Atherosclerosis, and Ischemic Heart Disease. Arch. Intern. Med., 1999, 159, 1542-48.

7. Taylor A.J., Kent S.M., Flaherty P.J. et al. Arterial biology for the investigation of the treatment effects of reducing cholesterol ARBITER. Circulation, 2002, 106(16), 2055-60.

8. Breuer H., Finchman Y., Hinrichsen P. et al. Coronary artery plaque rapidly induced by local electromagnetic stimulations in the baboon. Eur. Surg. Res., 1989, 21(2), 123-8.

9. Betz E., Schlote W. Responses of vessel walls to chronically applied electrical stimuli. Basic Res. Cardiol., 1979, 74, 10-20.

10. Chekanov V., Mortada M., Tchekanov G. et al. Pathologic and histologic results of electrical impulses in a rabbit model of atherosclerosis: 24 hour versus 8 hour regimen. J. Vasc. Surg., 2002, 35, 554-62.

11. Chekanov V., Mortada M., Maternowski M. et al. Slowed progression or elimination of atherosclerosis by low-frequency electrical impulses. J. Card. Surg., 2003, 18, 47-58.

12. Chekanov V.S. Low-frequency electrical impulses reduce atherosclerosis in cholesterol fed rabbits. Med. Sci. Monit., 2003, 9(8), BR302-309.
13. Hudlicka O., Brown M., Egginton S. et al. Angiogenesis in skeletal and cardiac muscle. Physiol. Rev., 1992, 72, 369-417.
14. Mosseri M., Izak T., Rosenheck S. et al. Coronary angiographic characteristics of patients with permanent artificial pacemakers. Circulation, 1997, 96(3), 809-15.
15. Jelic V., Belkic K., Djordjevic M., Kocovic D. Survival in 1431 Pacemaker Patients: Prognostic Factors and Comparison With the General Population. PACE, 1992, 15(2), 141-7.
16. Mattioli A.V., Rossi R., Annicchiarico E., Mattioli G. Causes of death in patients with unipolar single chamber ventricular pacing: prevalence and circumstances in dependence on arrhythmias leading to pacemaker implantation. PACE, 1995, 18(1 Pt 1), 11-7.
17. Pette D. Adaptation of skeletal muscle to increased neuromuscular activity as induced by chronic low-frequency stimulation. Scand. J. Rehab. Med. Supp., 1994, 30, 7-18.
18. Ferrara N. Vascular endothelial growth factor. Trend Cardiovasc. Med., 1993, 3, 244-250.
19. Folkman J. Clinical application of research on angiogenesis. N. Engl. J. Med., 1995, 337, 1757-63.
20. Annex B., Torgam C.E., Lin P. et al. Induction and maintenance of increased VEGF protein by chronic motor nerve stimulation in skeletal muscle. Am. J. Physiol., 1998, 274, H860-H867.
21. Hang J., Kong L., Gu J.W., et al. VEGF gene expression is upregulated in electrically stimulated rat skeletal muscle. Am. J. Physiol., 1995, 269, H1827-31
22. Diaz M., Frei B., Bita J. et al. Antioxidants and atherosclerotic heart disease. N. Engl. J. Med., 1997, 337, 408-16.
23. Smith C., Mitchinson M., Arnoma O. et al. Stimulation of lipid peroxidation and hydroxyl-radical generation by the contents of human atherosclerotic lesions. Biochem. J., 1992, 286, 901-5.
24. Lee T., Shiao M., Pan C. et al. Iron-deficient diet reduces atherosclerotic lesions in apo E-deficient mice. Circulation, 1999, 99, 1222-9.
25. Halliwell B. Use of desferrioxamine as a "probe" for iron-dependent formation of hydroxyl radicals. Biochem. Pharmacol., 1985, 34, 229-33.

Coronary artery aneurysm: three case reports.

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Summary

The article reviews the clinical versus angiographic results in three patients with coronary artery aneurysm.

Keywords

Coronary artery aneurysm, congenital anomaly of coronary artery, coronary artery atherosclerosis

Abbreviations.

CAA - coronary artery aneurysm
OMA - obtuse margin artery
LCA - left coronary artery
CxA - circumflex artery
RCA - right coronary artery
LAD - left anterior descending artery
FC - functional class

Introduction.

Coronary artery aneurysm (CAA) is a rather rare pathology, which is associated with ≥50% local dilatation of a coronary artery as compared to its proximal portion. Daoud reported the 1.4% incidence of coronary artery aneurysm among 694 autopsies of patients above 16. CAA most commonly affects RCA, and, in decreasing order, left main, LAD and CxA. Multiple CAA have also been reported (4).

Atherosclerosis is the most common cause of CAA (6). The second most frequently observed cause is congenital (5,8). In addition, coronary artery aneurysms occur after inflammatory disorders, such as Kawasaki disease (2); traumatic aneurysms of coronary artery following angioplasty attempt were reported (1).

The most accepted CAA classification is as follows (3,7):

I. Local aneurysm
  A. congenital aneurysm
  B. secondary aneurysm due to:
    1. atherosclerosis
    2. inflammation
    3. injury
    4. neoplasm
    5. arteriovenous fistula
II. Dissecting aneurysm
  A. primary aneurysm
  B. CAA secondary to thoracic aortic dissection
III. Diffuse arteriovenous fistula

Clinical significance of CAA is unclear. This condition is commonly asymptomatic or accidentally revealed. However, aneurysm is known to increase the risk of myocardial infarction; in some patients, including children, multiple CAA have been recognized as the only cause of angina (8). Coronary aneurysm ruptures causing hemopericardium, cardiac tamponade and death have also been reported.

We found CAA to be rather rare (this condition was revealed in 3 patients out of 1200, who underwent coronary angiography between 1996 and 2003). One patient presented with a giant congenital aneurysm of LAD with subtotal symptomatic RCA stenosis that resulted in large myocardial infarction causing cardiogenic shock and death. CAA revealed by coronary angiography was virtually asymptomatic in two patients. The three case reports are summarized below.

Case reports.

Patient M., male, aged 58, was admitted to CCU of Sechenov Medical Academy of Moscow. The patient presented with severe pain and signs of acute Q-wave inferior myocardial infarction on ECG (subacute stage). Within 4 hours after the admission the patient developed pulmonary edema and cardiogenic shock, therefore, an attempt of "life-saving" angioplasty was considered. Coronary angiography revealed balanced type of coronary circulation, intact left main artery, large coronary aneurysm of LAD (9.0

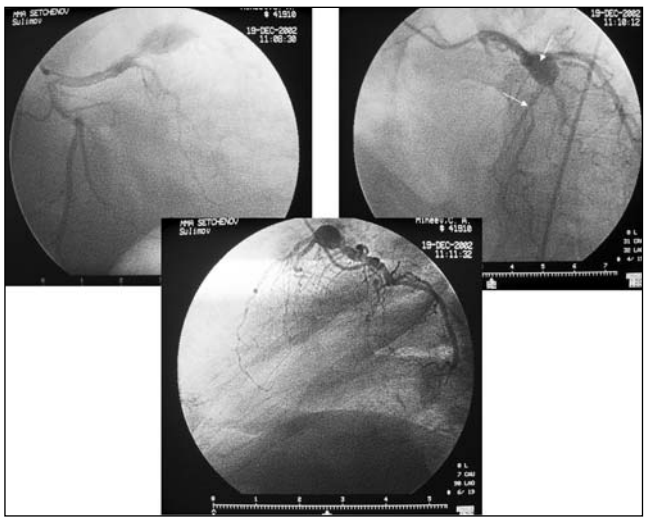

Figure 1.

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x 16 mm) with 80% stenosis of its distal portion (Figure 1). CxA was unchanged. RCA had a very large diameter (5.5 - 6 mm) and a 90% symptomatic stenosis in its proximal third (Figure 2).

Due to the clinical presentation (ECG signs of inferior myocardial infarction), as well as the impossibility

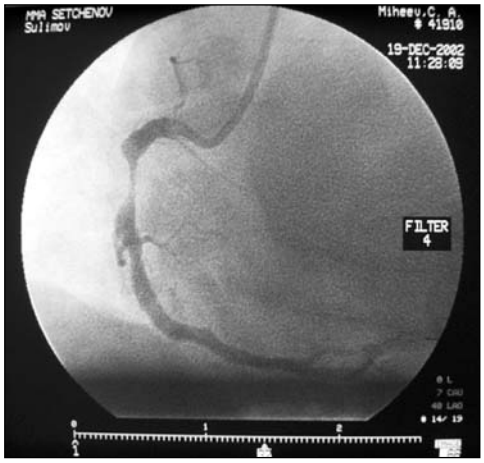

Figure 2.

of any manipulations near the giant aneurysm of LAD, the subtotal symptomatic stenosis of RCA was considered to be an infarction-related lesion. Emergency stenting of RCA was performed using Bx Velocity stent (Cordis, J&J, USA) 4.0 x 18 mm at 22 atmospheres (the resulting stent diameter was 4.6 mm). Angiographic success was achieved: TIMI III blood flow, no intimal dissection was present, ≤20% residual stenosis (Figure 3).

Immediately after stenting of RCA the patient's condition improved: pain was reduced, blood pressure

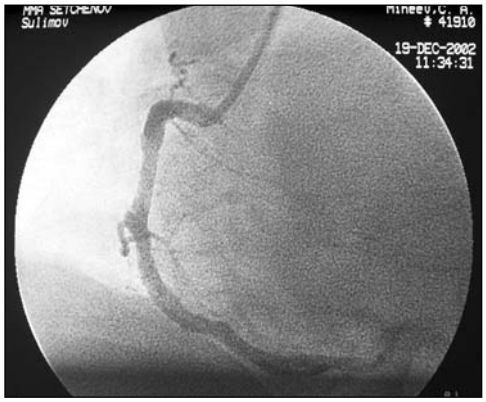

Figure 3.

remained stable at a level about 85/60 mm Hg. ECG showed reversal of ST elevation in II, III and aVF leads. At the same time, signs of left ventricular failure and oliguria were present.

Fourteen hours after stenting the symptoms of cardiogenic shock recurred. ECG showed ST depression in I, aVL and V4-V6 leads.

Despite the infusion of pressor amines (dobutamine, dopamine) and artificial lung ventilation symptoms of pulmonary edema and cardiogenic shock increased. Twenty hours after stenting persistent asystolia developed, which was associated with increasing signs of heart failure.

Autopsy revealed, that the LAD aneurysm was most likely of congenital origin (degeneration of muscular and elastic layers of vessel wall without any signs of atherosclerosis involving intima and media). Fresh thrombosis was observed in LAD proximal to the aneurysm. RCA stent was patent. Sites of myocardial necrosis were found in left ventricular posterolateral region.

Thus, as described above, the patient was most likely to have a giant congenital aneurysm of LAD, which had been asymptomatic until the development of an independent atherosclerotic lesion of RCA causing acute myocardial infarction. Large diameter of RCA indirectly confirms the assumption, that collateral vessels for LAD territory arose from RCA, thus maintaining adequate perfusion of the distal LAD portions. Abrupt decrease of blood flow in RCA due to acute thrombosis resulted in inferior myocardial necrosis, as well as severe ischemia of the entire left ventricle. The combination of these two conditions resulted in an incurable cardiogenic shock, which ultimately became the immediate cause of death.

Patient K., male, aged 72, presented with a 8-year history of coronary heart disease. In 1997 a 80% stenosis of the middle third of LAD was revealed by coronary angiography, which was performed for severe angina (III-IV FC). In addition, a saccular aneurysm of the middle third of CxA was found. The patient underwent balloon angioplasty and stenting of LAD (Palmatz-Shatz stent, Cordis, J&J). The symptoms of angina reduced, but in 2001 recurred again. Coronary angiography revealed a new 90% stenosis of the middle portion of RCA. Direct stenting was performed using Be-stent (Medtronic). Between 2001 and 2003 the patient was feeling well. In autumn 2003 he was admitted to the hospital with symptoms of chest pain that had no strict association with physical activity. The results of stress-test were uncertain, therefore, coronary angiography was repeated.

The study showed balanced type of coronary circulation, normally positioned stent in the middle portion of LAD with no signs of restenosis, a 6-7 x 8 mm saccular aneurysm of the middle portion of CxA, (Figure 4), normally positioned stent in RCA middle portion with no signs of restenosis.

Thus, this patient with multi-vessel coronary atherosclerosis had a combination of stenoses and an aneurysm. Both stenoses were symptomatic and caused angina, whereas the aneurysm of CxA

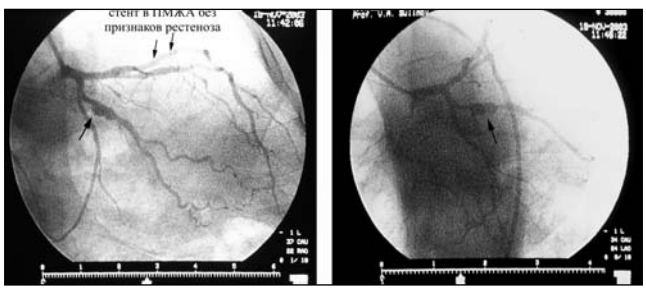

Figure 4.

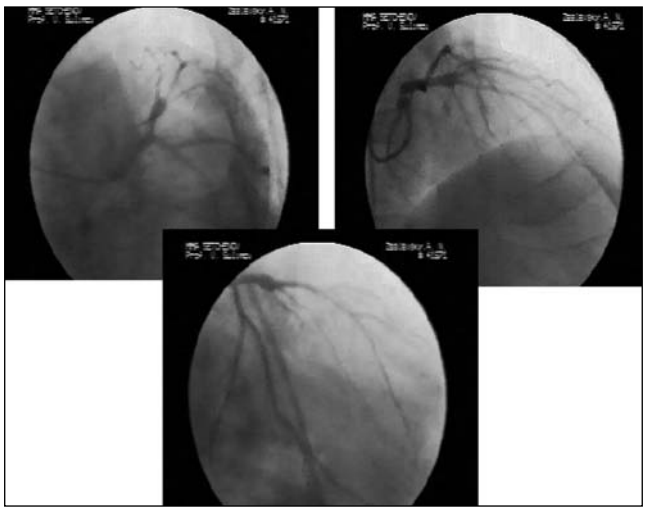

Figure 5.

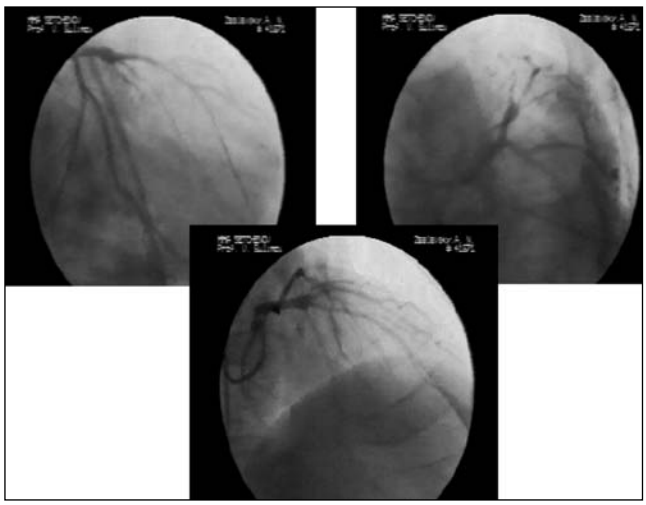

Figure 7.

remained asymptomatic during the entire 6-year follow-up.

Patient Z., male, aged 42, was admitted to Cardiological clinic with chest pain that had no strict association with physical activity and first occurred 4 weeks prior to admission. The results of stress-test were uncertain, myocardial Tc-scintigraphy revealed slightly impaired perfusion of the cardiac apex, which occurred during exercise. Considering the patient's age and sex, coronary angiography was indicated.

The study revealed balanced type of coronary circulation, a 6 x 7 mm aneurysm of proximal portion of the LAD, immediately distal to the aneurysm three equal small caliber branches arose from LAD (~2-2.5 mm, Figure 5). RCA was unchanged.

Therefore, the patient was most likely to have a congenital LAD aneurysm. The flow-limiting role of the aneurysm was doubtful. The patient is currently followed-up in the hospital.

Conclusion

To summarize these case reports we can conclude, that, despite the threatening angiographic appearance, CAA itself, as a rule, poses no danger to a patient. Thus, in the first case described above, the giant congenital aneurysm of LAD remained asymptomatic until the development of atherothrombotic RCA occlusion.

At the same time, the presence of an aneurysm in a single coronary artery certainly aggravates the prognosis in atherosclerotic patients, and, particularly, in case of atherothrombosis in another coronary artery. This is due to the lack of adequate collateral perfusion from the artery, where the flood flow is compromised by an aneurysm. In addition, the decreased blood flow distal to the aneurysm may provide insufficient perfusion of the corresponding territory, which is directly determined by the collateral blood flow from the other coronary arteries.

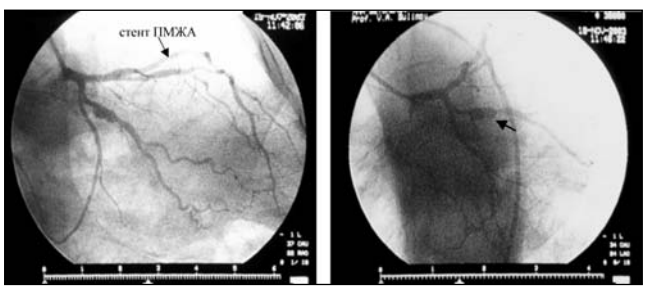

Figure 6.

Therefore, we believe that patients with CAA necessitate more careful follow-up to provide early diagnosis and treatment of atherosclerotic coronary stenoses. The follow-up must include periodic coronary angiography performed at least once yearly.

References:

1. A.M. Babunashvili, D.P. Dundua, D.S. Kartashov. Aneurysm of the left main following coronary angioplasty. Grudnaya I Serdechno-Sosudistaya Khirurgia, 1998, 3, 73

2. Yu.M. Belozerov, L.V. Bregel, A.A. Dzizinsky, V.M. Subbotin. Sudden cardiac death due to Kawasaki's disease. Rossiysky Meditzinsky Jurnal, 1999, 1, 43-45

3. Abrams' Angiography, Vv. I-III, Lippincot-Raven Publishers, 1997; V1: III-B-29

4. Daoud A.S., Pankin D., Tulgan H., Florentin R.A. Aneurysms of coronary artery: report of the ten cases and review of the literature. Am. J. Cardiol., 1963, 11,228

5. Dawson J.E. Jr, Elleson R.G. Isolated aneurism of the anterior descending coronary artery - surgical treatment. Am. J. Cardiol., 1972, 29,868

6. Eshchar Y., Yahini J.H., Deutsch V., Neufeld H.N. Arteriosclerotic aneurism of the coronary artery. Chest, 1977, 72,374

7. Kalke B., Edwards J.E. Localized aneurysms of the coronary arteries. Angiology, 1968, 19,460

8. McMastin D.E., Stoke A.J., Franch R.H. Multiple coronary aneurisms in a child with angina pectoris. N. Engl. J. Med., 1974, 290,669

Ulyanovsk regional clinical hospital department of interventional radiology

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The first angiography procedure was conducted in Ulyanovsk in 1974. Since that time and till 1997 all interventional radiology diagnostics and therapy were performed by the staff members of the Department of Interventional Radiology of the Regional Hospital. The Department of Interventional Radiology was founded in 1997 after the installation of Advantx LCV angiography machine (General Electric).

The total hospital's capacities consist of 1500 beds, among them:

- Vascular - 30;
- Cardiac surgery - 5;
- Cardiology - 80;
- Rhythm disorders - 20;
- Rheumatology - 40;

The Department of Interventional Radiology has no in-patient unit.

Major trends of activity.

All types of diagnostic procedures in adults and children are performed in the department. Therapeutic interventions include angioplasty and stenting of coronary and peripheral arteries (e.g., carotid and vertebral arteries); embolization of peripheral arteries and veins, as well as arteriovenous malformations, carotid-cavernous fistulas and cerebrovascular aneurysms; pacemaker implantation (single- and dual-chamber, mono- and bipolar pacing); radio-frequency ablation of conductive pathways; permanent or transient implantation of cava-filters; endosurgical management of biliary tracts, balloon esophagoplasty, cyst drainage and sclerotherapy in parenchimal organs, intra-disk ozone therapy, Hasser node hydrothermal destruction, various types of needle biopsy, removal of foreign bodies from soft tissues, vessels and heart.

Since 2002 interventions for congenital heart diseases have been performed, including balloon valvuloplasty of the pulmonary valve, balloon angioplasty of aortic coarctation, embolization of patent ductus arteriosus with guided Gianturco coils.

Unfortunately, we're lacking equipment for intravascular ultrasound, percutaneous rheolytical thrombectomy and vessel recanalization.

We are planning to set up endovascular closure of ASD secundum and VSD.

Table. Number of diagnostic and therapeutic procedures.

Year	Diagnostic procedures	Therapeutic procedures
2002	1695	306
2003	1122	247
First half of 2004	705	172

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DUPLEX SCANNING: PREDICTION OF THE POSSIBILITIES AND MONITORING OF THE RESULTS OF ENDOVASCULAR STENTING OF OCCLUSIVE LESIONS OF THE LOWER LIMBS' ARTERIES

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To evaluate the effectiveness of DS for the selection, prediction of the effectiveness and control of the results of endovascular stenting (ES from 2000 to 2003 duplex scanning (DS) of the lower limb arteries was performed in 422 patients. Technical possibility of ES and the prognosis of stent performance have been determined. 64 patients were selected for ES, a total of 72 stents was implanted: 35 in the iliac arteries, 28 - in the superficial femoral arteries, 2 - in the deep femoral artery, 4 - in the popliteal artery, 3 stents - in the area of anastomoses after bypass operations. Simultaneous implantation of 2 stents was performed in 8 patients. In 7 cases ES was combined with balloon angioplasty, in 6 cases - with regional thrombolysis or rheolytic thrombectomy. Balloon expandable stents were used in 58 cases, nitinol self-expandable stents - in 14 cases. Immediate results of ES were evaluated in 1-3 days, late results - in 1, 3, 6, 12 months and then yearly. Follow-up examination performed during the period of 3 months to 3 years.

The sensitivity of pre-operative DS was 93,7%. After the operation no residual stenoses of hemodynamical significance were revealed in the area of ES. Late post-procedural complications occurring later than after 3 months, were seen in 18 patients (28,1%). The rate of stents' restenoses/reocclusions in the aorto-iliac position was 11,4%, in femoro-popliteal position- 15,6%, the rate of arterial lesions in the contralateral limb, in proximal or distal parts of the vascular bed - 14%. This fact suggest the necessity of multiple repeated ultrasonic examinations of the lover limb arterial system in whole. While assessing the restenoses we considered in-stent peak systolic velocity gradient > 2 as hemodynamically significant. Repeated endovascular procedures (a total of 15 procedures) were performed in 10 patients.

DS is sufficiently effective for the selection of patients, predication and monitoring of the results of ES.

OVERDRIVING ATRIAL PACING FOR LOCAL ISCHEMIA REVEALING DURING PTCA FOR MULTI-VESSEL LESION

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At present PTCA is an effective and safe method of treatment not only for isolated stenoses of the coronary arteries, but also for multiple lesions.

In some cases, however, the physician faces the problem of the determination of indications as for the volume of the performed intervention. In single-vessel lesion, whose hemodynamical significance is doubtful, the revealing of myocardial ischemia with functional methods allows in most cases to solve the question of performing the intervention. In the presence of multivessel disease those methods don't allow to determine with certitude which of the arteries is responsible for ischemia, or whether it is necessary to revascularize each of those arteries

It is related to the fact that in multi-vessel coronary lesion the presence of a "significant" stenosis in one of the main arteries, for example, in LAD, causes clinical and ECG-signs of ischemia mainly in in the region supplied by this artery, thus limiting the possibilities of detecting myocardial ischemia in the regions supplied by other arteries, for example, RCA, whose stenosis is of doubtful hemodynamical significance.

In order to solve this problem we suggest the method of intraprocedural revealing of ischemia using overdriving atrial pacing.

For this purpose, after the elimination of the "main" angiographically significant stenosis we induce overdriving atrial pacing, allowing for the evaluation of hemodynamical significance of a "doubtful" stenosis. In cases of the appearance of clinical or ECG-signs of ischemia revascularization is indicated.

Intravascular ultrasonic investigation is indicated for the determination of the diagnostic value of angiographic method and for more precise diagnostics of the degree of coronary lesions.

ENDOVASCULAR TREATMENT OF MULTIFOCAL ATHEROSCLEROSIS

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The determination of indications and the choice of the sequence of reconstruction in multifocal atherosclerotic lesions of different arterial beds in patients with lower limb ischemia causes a lot of difficulties.

During the last 3 years in order to precise the localization and the degree of stenosis as well as to choose the method and the strategy of treatment for multifocal atherosclerosis in patients aged over 45 years with lower limb ischemia, at the time of aortography, we have performed coronary angiography and, when necessary, selective angiography of the renal arteries.

During the last 2 years we have operated on 42 patients with multifocal occlusive-stenotic lesions of different arterial pools using transluminal balloon angioplasty (TLBA) with stenting. The presence of hemodynamically significant stenoses in patients with lower limb ischemia, in which the restoration of the normal blood supply is indicated, at the first stage the restoration of coronary and renal arterial blood flow was performed. 4-5 days after the restoration of adequate blood flow in the vital organs, it was possible to perform TLBA and stenting of lower limb arteries.

We evaluated immediate and late results of this approach.

In 8 cases we performed TLBA and stenting of the coronary arteries and the aortic branches (renal and iliac arteries). Seven patients underwent TLBA and stenting of the renal arteries and the lower limb arteries. In 34 patients we performed TLBA and stenting of the lower limb arteries at different levels (iliac segment and femoro-popliteal segment).

Mean duration of hospital stay was 10 ±2.3 days.

Cumulative patency rate of all the arteries submitted to TLBA and stenting during 1 year was 97.6%.

Early postoperative complications occurred in 2.38% of cases.

Late postoperative complications, in the form of hemodynamically significant re-stenoses (lumen narrowing > 50%), 6 months - 1 year after the procedure, occurred in 16,5% of cases in a separate group of patients. Most patients with re-stenosis of the stented segment underwent repeated TLBA with good late results.

The results obtained during this 2-year period allow to recommend a wider use of the method of transluminal balloon angioplasty with stenting in patients with multifocal atherosclerotic lesions of different arterial regions.

USE OF CAVA-FILTER "OSOT" FOR THE PREVENTION OF PULMONARY ARTERY THROMBOEMBOLISM (PATE)

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To evaluate anti-embolic effectiveness of cava-filter "Osot" in clinical settings this cava-filter was implanted in 250 patients. The indications for the implantation were: massive and sub-massive pulmonary embolism (PE) in 47 pts, floating thrombi in the inferior vena cava system in 83 pts, combination of PE and deep vein thrombosis in 120 pts. 224 "Osot" cava-filters were implanted in infra-renal position, while in 26 cases filters were implanted cranially to the ostia of the renal veins. In 12 cases supra-renal implantation was indicated because of pregnancy, in 14 - because of inferior vena cava thrombosis extending up to or proximally to the ostia of renal veins. The implantation was carried out via femoral approach in 67 pts, via subclavian and jugular veins - in 183 pts.

16 patients (6,4%) died in early postoperative period. Recurrent non-fatal PE revealed in 3 pts (1,2%) was due to the distal migration of cava-filter "Osot" into the common iliac vein caused by large inferior caval vein (so called Megacava). The embolism in the cava-filter was revealed in 19 out of 250 pts (7,6%) However without no signs of acute ileo-caval occlusion. Thrombolytic therapy for PE was carried out in 113 pts (45,2%). The results were judged as good in 81 cases (72%), satisfactory in 27 (24%), and non-satisfactory in 5 cases (4%).

Thrombolytic therapy for acute deep veins thrombosis of the lower limbs was carried out in 29 pts. In 26 of them (90%) the results were judged as good and satisfactory.

We didn't see recurrent PE related to the use of cava-filters in patients who received fibrinolythic therapy

Our results demonstrate the high efficacy of "Osot" cava-filters for the prevention of pulmonary artery thromboembolism.

THE USE OF NEW STENT OF NITINOL MONOTHREAD FOR THE CREATION OF PERCUTANEOUS TRANSHEPATIC PORTO-SYSTEMIC SHUNTS

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New Nitinol stent was implanted in 14 patients with liver cirrhosis aged 34 - 64 years (mean. 40,1 ± 8,1 years) for creation of intrahepatic porto-systemic shunts. Before the procedure blood pressure in the portal vein was 17 - 39 (mean 28,9 ± 7,1) mm Hg. Stent diameter was 12 mm, its length varied from 48 to 80 mm. Shunt permeability was controlled with ultrasonic methods 5-7 days after the intervention. Follow-up duration was 36,6 ± 26,2 months in average.

In one case stent dislocation was noticed. Blood pressure in the portal vein after the procedure was 6,0 - 28,0 (mean 20,8 ± 5,9) mm Hg. During the follow-up shunt occlusion was revealed in one patients, stenotic changes in the anastomotic region lead to four repeated interventions.

New stent design makes it convenient for use and effective for the formation of porto-systemic junction.

ENDOVASAL PREVENTION OF PULMONARY ARTERIAL EMBOLISM

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We performed the analysis of the effectiveness of implantation of intravenous cava-filters "Sand-glass - M".

Triplex US-scanning (ALOKA SSD 2000, Japan), distal phlebography, retrograde ileo-cavagraphy were performed.

We have analyzed the results of treatment of 27 patients from the Department of vas-cular surgery, who underwent the implantation of intravenous cava-filters "Sand-glass - M" for the prevention of PE and its recurrence from 2001. There were 14 (51,8%) females and 13 (48,2%) males, 81,8% of patients were socially active.

Following proximal localization of thromboses were revealed: inferior vena cava (IVC) in 9 patients (33,3%), iliac veins (IV) - 9 (33,3%), femoral veins (FV)- 6 (22,2%), popliteal veins (PV) - 3 patients (11,2%). The rate of recurrence in different venous thromboses' lo-calization was: IVC - 42,9% (4 patients), IV - 71,4% (6 patients), FV - 83,3% (5 patients), PV - 66,6% (2 patients).

The distribution according to the type of thrombosis: parietal thrombosis - 15 patients (55,6%), floating- 11 (40,7%), occlusive thrombosis- 1 (3,7%).

The implantation of cava-filters was carried out following standard indications and methods developed in the clinic of faculty surgery of Moscow State Medical University headed by Academician V.S. Saveliev: floating and parietal thromboses and recurrent PE.

The mortality was 0%. There were no cases of PATE, its recurrence and cava-filters thromboses. IVC thrombosis was revealed in 1 case (3,7%). Control ultrasound examination revealed thrombotic masses in the cava-filter's "trap" in 2 patients (7,4%).

Our results allow us to conclude that the implantation of intravenous cava-filter "Sand-glass - M" is a highly effective method for the prevention of PE and its recurrence.

MINIMALLY INVASIVE SURGERY IN THE TREATMENT OF DECOMPENSATED FORMS OF CHRONIC VENOUS INSUFFICIENCY OF THE LOWER LIMBS

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We present our experience with the use of endoscopic method for the revision of sub-fascial space and the dissection of perforating veins of the leg combined with other types of surgical interventions in patients with chronic venous insufficiency of the lower limbs of IV - VI clinical class (CEAP, 1995), with the account of the particularities of blood supply in the leg's epifascial tissues.

From 1998 till 2002 we have operated on 57 patients aged 25-76 years, among them 41 with post-thrombotic disease and 16 with varicose disease. They underwent subfascial endoscopic dissection of the communicating leg's veins according to the selective method in combination with phlebectomy and sclerotherapy of the saphenous vein trunk according to our method. Endoscopic subfascial dissection of communicating veins was performed with the use of standard equipment for laparoscopic interventions (K. Storz). During the operation the perforating bundle was exposed subfascially, the perforating vein was transsected with electrical surgical means, the remaining elements of the bundle were preserved (Invention license of the RF № 2195877).

In post-operative period we observed the regress of trophic disorders, active healing of ulcers, there were no cases of the wound edge necrosis or of the superficial nerves' damage. Trophic ulcers were healed in 7-18 days. 43 patients were followed for 1-4 years, the results of complex treatment were judged as good in 14 (32,6%), as satisfactory in 27 (62,8%), as non-satisfactory in 2 (4,6%) of them.

Thus, endoscopic separate selective dissection of perforating veins is a radical, low-traumatic, anatomically and functionally justified method for the elimination of perforating shunting, and its combination with intraoperative catheter sclerotherapy allows to decrease significantly the rate of postoperative complications and the duration of in-hospital stay in patients with chronic venous insufficiency of the lower limbs.

RESULTS OF DRUG THERAPY FOR CRITICAL ISCHEMIA OF THE LOWER LIMBS

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To improve the results of treatment of critical lower limbs ischemia using serotonin adipinate we have studied 70 males with peripheral artery disease at the stage of critical ischemia. Drug therapy included serotonin adipinate (license №2201262, 27.03.2003). Mean age of patients was 58,4 years, mean duration of the disease - 6,4 years. Lover limb grade III ischemia was noticed in 46% of patients, the grade IV - in 54% of patients. We have studied their clinical characteristics and analyzed the results of rheovasographic investigations (Rheo-Spektr NS 1005, Neurosoft, Russia), ultrasonography (LOGIQ-500 PRO Siries, General Electric), capillaroscopy (capillaroscope M-70 A, Russia), skin thermometry (thermometer TPEM-1), acid-base state (capillary and venous blood, taken from the 1st finger of the ischemic limb) (AVL-995, Austria), etc. before and after treatment.

In early post-treatment period good results were achieved in 40%, satisfactory results in 37% patients. The lack of improvement was noticed in 20%, while ischemia progress with further deterioration - in 3% of patients. Amputation had to be performed in 8 patients (11,4%): in 2,9% - at the level of the middle third of the thigh, in 4,3% - at the level of the middle third of the leg, in 4,3% - with the preservation of the supporting function of the foot.

In the long-term follow-up positive initial results of the treatment persisted in 67,7% of patients, while ischemia progressed and led to the amputation at the thigh level in 6,2% and on the leg level in 4,6%, with subsequent re-amputation at the thigh level in 1,5%.

The use of serotonin adipinate for the treatment of critical lower limbs ischemia allows to improve early and late results of treatment, to lower the rate of amputations.

TYPES OF CAROTID LESIONS AND SURGICAL TACTICS

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To study the surgical approaches in different variants of carotid pathology we analyzed our experience with the treatment of 127 patients with carotid lesions during the last three years (2001-2003). Surgery was performed in 99 patients. Among them there were 65 (65,7%) patients with atherosclerotic stenotic lesion (stenosis > 65%), 22 patients (22,2%) had hemodynamically significant tortuosity of the carotid arteries. The association of internal carotid artery stenosis and its pathological tortuosity was seen in 5 cases. Hemodynamically significant atherosclerotic lesion of carotid and subclavian arteries was revealed in 5 cases. Two patients had aneurysms of carotid artery bifurcations associated with internal carotid artery stenosis.

Surgical interventions were carried out under conduction anesthesia in 29 cases, under general anesthesia in 70 cases. Temporary carotid bypass was used in 2 patients.

The patients with stenotic atherosclerotic lesions of the carotid arteries underwent: eversion endarterectomy in 37 cases, open endarterectomy in 17 cases, combined with patch placement in 6 cases, with carotid-subclavian bypass in 5 cases. In one case endarterectomy was combined with aorto-coronary bypass grafting. In cases of pathological tortuosity we used the resection of internal carotid artery in 17 patients, of common carotid artery in 5 patients. Patients with combined lesions (kinking + stenosis, aneurysm + stenosis) underwent eversion endarterectomy combined with the resection of internal carotid artery.

In our series atherosclerotic lesion was the leading cause of carotid lesions - 65,7%, the second place belongs to the pathological tortuosity of the carotid arteries - 22,2%, combined lesions account for 12,1%. At present the direct surgical correction is the leading method for the treatment of carotid pathology. In cases of combined kinking, aneurysms, occlusion of ipsilateral subclavian artery it is reasonable to extend surgical intervention for total correction of all the lesions.

RESULTS OF PTCA IN PATIENTS AFTER ORTHOTOPIC HEART TRANSPLANTATION

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Autoimmune processes are mainly responsible for stenotic lesions of the coronary bed in patients after orthotopic heart transplantation. From 1998 till 2004 we have followed 8 patients after orthotopic heart transplantation. All those patients underwent coronary angiography and myocardial biopsy every 6 months. If hemodynamically significant stenoses of the coronary arteries were revealed the patients were submitted to PTCA. Four patients had multi-vessel diseases, in 4 cases minor changes of coronary arteries were found. A total of 15 PTCA was performed during the follow-up period in 4 patients. One patient underwent PTCA of the obtuse marginal artery with stable angiographic result in the late follow-up (over 1 year). Another patients underwent PTCA of left anterior descending and circumflex arteries at different times and with good long-term angiographic result (over 2 years).

During the follow-up period frequent aggravation of autoimmune processes (as judged by myocardial biopsy data) was noticed in 2. Coronary angiography in those patients revealed multi-focal lesions of the coronary bed. The first patient underwent 5 PTCA of different segments of LAD, the second - 3 PTCA of : LAD and 5 PTCA of the diagonal branche. Along with stable long-term angiographic results after PTCA (from 10 to 25 months) those patients were found to have new stenoses in other segments of the coronary arteries and diffuse narrowing of the distal lumen, necessitating repeated PTCA. In all cases good angiographic results were achieved (residual stenosis up to 30%), the procedures were carried out without complications.

We revealed long-term preservation of good results after PTCA in such patients, but at the same time new stenoses were continuously formed in other coronary segments. Thus, to our opinion, in patients after orthotopic heart transplantation it is reasonable to use PTCA without stenting.

EVALUATION OF THE EFFECTIVENESS OF ENDOVASCULAR OCCLUSION OF HEMANGIOMAS WITH COMPLEX ANATOMICAL LOCALIZATION IN CHILDREN BY CEREBRAL OXYMETRY

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Endovascular occlusion is one of the methods used in endovascular surgery and represents a mean for the lowering or the blockade of regional blood flow by infusion of embolizing materials. While performing such manipulations we evaluate brain oxygen status using the method of optic spectroscopy in para-infrared diapason (Critikon RedOx - 2020 "Jonson&Jonson", INVOS-5100).

We studied 20 patients aged from 3 months to 3 years who underwent endovascular occlusion of the hemangiomas of complex localization, supplied by external carotid artery.

Our study revealed sinusoid character of the curve of regional saturation (RSat) during embolization. During embolization the curve RSat returns to baseline values, suggesting the total cessation of hemangioma supply with blood, that is, the success of embolization.

That type of monitoring allows for successful follow-up of hemodynamic changes in the brain, occurring during contrast dye infusion and embolization. Thus, monitoring of oxygen status allows to reduce significantly the volume of contrast agents, to control the volume of the infused embolizing materials and to decrease x-ray exposure of patients.

IMMEDIATE CLINICAL AND ANGIOGRAPHIC RESULTS OF ENDOVASCULAR CORONARY PROCEDURES IN PATIENTS WITH THE HISTORY OF SURGICAL MYOCARDIAL REVASCULARIZATION.

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Aim of the study: to evaluate immediate clinical and angiographic results of endovascular procedures (EVP) for the lesions of native coronary arteries, venous and arteriovenous grafts in patients with the history of aorto-coronary and/or mammaro-coronary bypass grafting (CABG and MABG).

Materials and methods: the study population consisted of all 24 patients (mean age 62±7,2 years; 22 (91,6%) males), who underwent 31 EVP (27 stentings and 4 PTCA) during the period from January 2001 till December 2003. All the patients had the history of CABG and/or MABG. The average "age" of the grafts was 14±9,3 months - from 2 months to 12 years. Clinical status of the patients corresponded to II-IV NYHA class. EVP were performed on: 7 arterial grafts ("the body" and the distal anastomosis of the internal mammary arterial graft in situ - 2 and 1 cases, respectively, the ostium and the distal anastomosis of the free arterial aorto-coronary graft - 2 cases both); 11 venous grafts (6 cases of EVP in the "body", 3 and 2 cases in the ostium and in the area of distal anastomosis of aorto-coronary venous grafts, respectively); 12 native coronary arteries (9 cases - distal to the anastomosis of the unchanged aorto-coronary graft; 3 cases - graft failure in native grafted arteries; 1 - LCA trunk with the passage to the ostium of the CxA in failed graft to CxA.

Results: satisfactory immediate angiographic results were achieved in all cases. There were 2 cases (6,5%) of transitory hemodynamically significant spasm of the arterial graft, resumed after selective infusion of nitroglycerine solution and IV adalate infusion. There were no major cardiac events in the studied group. The improvement of clinical status, presented as the decrease of angina severity by 2 classes and more, was seen in all the patients.

Conclusions: EVP are clinically effective and safe in patients with the history of direct surgical myocardial revascularization.

DIFFERENT METHODS OF SCLEROBLITERATION IN MODERN PHLEBOLOGY

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Sclerotherapy is a widely accepted method in modern phlebology. However, indications, tactics and priorities of different methods of sclerobliteration remain uncertain.

During the last three years we have performed phlebo-sclerobliteration in 725 patients for the following indications:

- Presence of teleangictasias and reticular veins;
- Intraoperative catheter obliteration of smaller veins;
- Postoperative sclerobliteration of smaller veins;
- Sclerobliteration under the Doppler ultrasonographic control of (echo-phlebo-sclerobliteration).

We used echo-phlebo-sclerobliteration in the following cases:

- In the presence of marked decompensated forms of chronic venous insufficiency when surgical intervention was impossible;
- As pre-operative preparation in patients with marked decompensated forms of chronic venous insufficiency;
- As a mean of postoperative care, if it has been impossible to liquidate local veno-venous reflux for some reasons;
- In the cases of recurrent varicose disease.

During the last three years we have performed sclerobliteration of tele-angiectasias and reticular veins in 564 patients, intraoperative and postoperative sclerobliteration in 67 patients.

We have performed 107 procedures of echo-phlebosclerobliteration in 94 patients. 44 patients had non-healing trophic ulcers of long duration.

We performed echosclerobliteration of perforating veins in 98 cases and of saphenous veins - in 9 cases.

Among 41 cases of venous trophic ulcer (with horizontal venous reflux in 24 cases), 12 patients underwent autodermoplasty. In 10 cases the flap healed safely. In all three cases of vertical venous reflux the ulcers were healed.

Sclerobliteration is a safe procedure, leading to a very small percentage of complications when used properly.

TRANSCORONARY ALCOHOL ABLATION OF VENTRICULAR SEPTUM IN OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY

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The aim of the investigation consisted in the study of the effectiveness of transcoronary alcohol ablation of interventricular septum (IVS) in patients with obstruic-tive form of hypertrophic cardiomyopathy (HCMP).

7 patients with HCMP (II-IV NYHA class) underwent transcoronary alcohol abla-tion of IVS. The diagnosis was established using transthoracic and transesophageal EchoCG, magnetic resonance tomography, ventriculography with left ventricular (LV) manometry. Percutaneous transcatheter alcohol ablation of IVS consisted in dosed non-surgical reduction of the mass and the contractility of hypertrophied myocardium at the base of IVS, responsible for the formation of subaortic LV obstruction, by the means of controlled alcohol occlusion of the first septal branch of LAD. The procedure was carried out with preventive placement of an endocardial lead for temporary pacing, pressure gradient monitoring, coronary angiography, intraoperative EchoCG.

Results:

Characteristics	Baseline data	Immediate result	Result after 6 months
NYHA class	2,9±0,4	1,1±0,1	1,1±0,1
LV/Ao gradient, mm Hg: at rest	80±21	21±7	15±7
Post-extrasystolic	108±35	31±9	19±9
EDP, mm Hg	19±4	16±4	12±3
LVEF, %	73±5	65±4	68±3
IVS thickness, mm	25±6	-	16±3
Mitral insufficiency	2,2±3	-	1,8±4

Discussion. LV outflow tract obstruction is the most important factor influencing the progress of heart failure and the survival in patients with HCMP. The drugs with negative inotropic action give a symptomatic effect without affecting significantly the course of the disease. Myoseptectomy and other surgical interventions lead to signifi-cant gradient decrease in the majority of patients, however surgical mortality varies from 2% in young patients to 17% in patients over 65. With DDD-pacing the gradient is only partially eliminated. Our results demonstrate that transcatheter alcohol ablation of IVS is highly effective in subaortic LV obstruction, is rather safe with proper methodical use and forms a solid alternative to previously used methods of treatment for obstruictive HCMP.

A CASE OF SUCCESSFUL REHABILITATION OF A PATIENT WITH CORONARY STENTING AT THE BACKGROUND OF DIFFUSE LESION OF THE CONNECTIVE TISSUE

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We present a clinical case of a successful rehabilitation of a patient after coronary stenting for acute myocardial infarction at the background of connective tissue disease (systemic lupus erythematosus).

55 years old female patient was hospitalized at day 4 after PTCA with stenting of the RCA performed in the 3rd Vishnevsky Central Military Hospital . At the age of 38 she was diagnosed to have dermatomyositis, and subsequently systemic lupus erythematosus developed. She took prednizolone (30-40 mg) for 17 years. The first anginal attack occurred on 31.12.03, the patient underwent thrombolytic therapy, then the signs of early postinfarction angina and heart failure developed. Coronary angiography revealed 80-90% stenosis in the middle segment of RCA. Emergency procedure was carried out on 02.02.04, and on day 4 the patient was transferred to the sanatorium "Arkhangelskoye" for rehabilitation. During the first days gastrointestinal, reperfusion, psychopathological and hypodunamical syndromes persisted. With the account of concomitant pathology dry-air carbon baths, medical physical exercises and dosed walks were used. Physical factors were limited. The patient received beta-blockers, statines, antiaggregants, glycocorticoids and delagil.

General state improved, motor activity and working capacity increased, indices of hemodynamics were stabilized, the manifestation of heart disease after the procedure were reduced which contributed to the improvement of the quality of life.

This example is an evident demonstration of the possibility of rehabilitation of severely ill patients after coronary stenting at the background of the suffered myocardial infarction and with concomitant connective tissue disease.

OVARIAN VEINS OCCLUSION IN THE TREATMENT OF PRIMARY VARICOSE OF PELVIC VEINS

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The aim of the study was the investigation of the results of ovarian vein occlusion in 148 women aged 18-45 years with primary varicose of the pelvic veins (PVPV), due to the valvular insuffcicenly of the ovarian veins. The women applied for medical assistance because of algomenorrhea, disturbances of menstrual cycle and sterility. PVPV was diagnosed using transvaginal sonography and Dopplerography during Valsalva maneuver, left-sided renal and phlebovaricography, as well as on the base of hormonal status of the patients. The following hormones were studied in the peripheral blood at the day +5 +7 of menstrual cycle: follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), progesterone (P), prolactine (PRL), testosterone (T). The occlusion of the left ovarian vein was carried out segment-by-segment using spiral-sclerotherapeutic method. Follow-up was carried out after 1 - 12 months with the use of ultrasonography and functional hormonal diagnostic tests. It is worth to notice that in 94 % of cases PVVSP was associated to some gynaecological pathology, predominantly with chronic inflammatory diseases of the uterine appendages. According to ultrasonography bilateral venous changes were revealed in 84,6 % of cases. The diameter of pelvic veins was 6 -13 mm. Phlebography revealed a "vicious" venous outflow through the right ovarian vein in 41,2% of women, while in 21% of them total disintegration of venous pelvic blood flow was revealed. The hormonal diagnostic tests revealed reliable decrease of FSH, LG, E2, P and T and the increase of PRL in 87% of patients as compared with the control group (n = 30) of healthy women. Follow-up after ovarian veins occlusion showed the decrease of vein diameter to 3 - 4 mm in 98% of cases, algomenorrhea resumed totally in 84% of women, menstrual cycle was normalized in 51% of patients; maximal effect was achieved by the 9th month of follow-up. The normalization of hormonal status was evident by the end of the 1st month with subsequent improvement of values by the 6th month post-treatment. Dynamic ultrasonography at 9 -12 months after the procedure - showed the normalization of ovarian structure with layers' differentiation. Thus, our studies allow to consider PVPV as a disease of ovarian veins with secondary disturbances of the hormonal status. It is evident that drug therapy of ovarian hypofunction without the correction of hemodynamical disturbances is without perspectives. Endovascular correction is a highly effective method in such cases and is indicated for the prophylactics of menstrual disorders, sterility, as well as for the elimination of pelvic pains.

UTERINE ARTERIAL EMBOLIZATION - A NEW METHOD FOR THE TREATMENT OF UTERUS MYOMATA

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To determine the effectiveness of uterine arteries embolization in the treatment of patients with uterus myomata 10 women aged from 38 to 46 years were operated on. Transvaginal ultrasound examination with the evaluation of the blood flow in the uterine arteries had been performed before the operation. After pelvic arteriography the 5F "Terumo" catheters were introduced into the left and the right uterine arteries. PVA particles of 300-500 mkm in diameter were used as embolizing material (dose up to 200 mg). Pain syndrome, hyperthermia and bloody discharges were assessed after the procedure. Dynamical examination was carried out 3, 6, 9 and 12 months after the procedure.

Before the operation the patients complained of periodical pains in the lower parts of the abdomen, of massive and prolonged menstruations. Secondary anemia was revealed in 72% of patients. Uterus increase corresponded to 6-10 weeks of pregnancy due to the nodes with 34-64 mm in diameter, with intermuscular (40%) and intermuscular-subabdominal (60%) localization. X-ray exposure time was 17 min. The course of postoperative period was characterized by the presence of pain syndrome during in average 22,25 hours. Subfebrile temperature appeared in 10-32 hours and lasted for 3-5 days. In 75% pf patients there were poor discharges from the vagina. 6 months after the procedures all of them noticed a significant decrease of the pain syndrome. Average duration of menstrual bleeding decreased to 6,6 days. According to the data of ultrasound examination, the regress of the nodes' dimensions made 30% of the initial size 9-12 months after the procedure.

Thus, the uterine artery embolization is a method of choice for the treatment of uterine myomata. While selecting the patients for this procedure one must prefer those with intramurally localized small nodes.

NEW HEPARINE-CONTAINING BIOPROSTHESES FOR SMALL ARTERIES

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To improve the results of small arteries replacement by the use of bioprostheses with heparin-containing covering. 194 samples of bioprostheses preserved with 0,625% solution of glutaraldehyde. The bioprostheses in the 1 group were modified with the use of heparin solution, in the 2 group - with aminoacid-heparin complex according to an original method.

We determined the amount of bioprosthesis-induced hemolysis, the amount of adsorbed albumin and immobilized heparin on bioprostesis' surface; the degree of complement system activation by bioprosthesis. We also studied the number of postoperative thromboses in acute and chronic experiments "in vivo" with bioprosthetic replacement of abdominal aorta in 47 cats.

It was shown that the use of aminoacid-heparin composition for the processing of bioprostheses allows to improve their hemocompatibility and thromboresistance. Thus, the quantity of heparin on bioprosthesis surface with aminoacid-heparin processing amounted to $50 \pm 0,07$, this value being several times higher than in the baseline ($0,23 \pm 0,05$) and heparinized ($0,29 \pm 0,02$) samples. We didn't see any case of thrombosis in bioprostheses treated with aminoacid-heparin complex 2 hours and 3 days after the operation, in difference with the control group where thrombosis developed in 100% of cases within 2 hours.