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Contents

Does Endovascular Perfusion Performed Within the First Hours after the Onset of the Disease Affect In-Hospital Prognosis in Q-wave AMI Patients?

E.T. Machitidze[1], I.Y. Kostyanov, A.G. Koledinsky, D.G. Iosseliani
City Center of Interventional Cardioangiology, Moscow, Russia

In spite of significant successes achieved in diagnostics and treatment of acute myocardial infarction the in-hospital mortality from this disease in our country remains significantly higher than in many other countries with highly developed healthcare system (1, 5, 14). To a large extent it is due to insufficiently wide and common use of new effective methods of diagnostics and treatment of acute myocardial infarction (AMI). Selective coronary angiography and angioplasty of coronary arteries would be the example. It is generally accepted that the former is the most precise method of coronary lesion diagnostics, while the latter is an effective method for the restoration of damaged heart blood supply (2, 3, 4, 12). Nevertheless, these methods are used in approximately only 5% of patients with acute myocardial infarction in Moscow, while in the other regions of Russia the statistics is even less reassuring (6). Meanwhile, by the most conservative estimate approximately 75-80% of patients with AMI require such procedures within the first hours of the disease. There are many reasons for such low medical activity concerning the use of modern effective treatment methods for AMI. These are the lack of special equipment and skilled staff in many hospitals, inadequate funding, etc. But even in this situation, the number of the above mentioned diagnostic and therapeutic procedures might be increased at least two-fold if desired by healthcare organizers and practicing physicians. However, to achieve this, it is necessary to recourse to evidence-based medicine more often, and to show specific examples of benefits and disadvantages of different treatment and diagnostics methods. In accordance with the above, we have set a goal to perform a comparative analysis of in-hospital treatment results in two groups of patients with Q-wave AMI: a) group of patients who received endovascular myocardial revascularization within the first hours after the onset of the disease, b) group of patients who did not received such treatment. In other respects the compared groups did not differ significantly by baseline status as well as by extent and localization of myocardial lesion and by conducted medical treatment.

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CLINICAL CHARACTERISTICS OF PATIENTS AND METHODS OF THE STUDY

Eight hundred sixty four Q-wave AMI patients treated in the Moscow City Center of Interventional Cardiology in the period from October, 2004 to October, 2007 were included in this study. The protocol of diagnostics and treatment of Q-wave AMI patients did not changed significantly during this time period, i.e. it was the same for these patients.

The patients were divided into two groups depending on the treatment strategy. The first group consisted of 529 patients who underwent urgent or semi-urgent selective coronary angiography and therapeutic endovascular procedures to achieve a myocardial reperfusion together with common methods of diagnostics and treatment. In the majority of cases (70.3%) these procedures were performed within the first 6 hours of the disease. In other patients the procedures were performed later during in hospital stay. The early post-MI angina and other clinical and laboratory signs of continuing myocardial hypoxia were the indications for procedure delay.

The second group consisted of 335 Q-wave AMI patients who did not underwent selective coronary angiography and endovascular therapeutic procedures due to different reasons (patients' refusal, intolerance of iodine being a part of contrast agents, lack of functioning angiography service during vacations or some holidays).

There were no significant differences between the compared groups in baseline clinical, laboratory and historical data (Table 1).

AMI diagnosis was established according to WHO criteria based on the complex of clinical data, electrocardiography results, pathological increase of the concentration of cardiospecific blood enzymes and EchoCG-evidenced presence of asynergy areas (in patients without AMI history). During data analysis a history of previous myocardial infarction, diabetes mellitus, arterial hypertension were taking into consideration. In the Cardiac ICU the patients with AMI were treated according to the protocol adopted in our Center including nitrates infusion and β-adrenoblockers, platelet aggregation inhibitors, ACE inhibitors, in some cases calcium channel blockers according to the protocol. Pre-hospital systemic thrombolysis was performed in a part of patients (n=141). In the first group the number of such patients was slightly higher.

Patients of the group 1 admitted to the hospital within the first 6 hours from angina attack onset under-

Table 1. Baseline Clinical Characteristics.

PARAMETER	GROUP 1 endovascular treatment (n=529)	GROUP 2 medical therapy (n=335)	p
Age. years	54.6±9.2	56.1±10.3	>0.05
Male gender	456 (86.2%)	273 (81.5%)	>0.05
Arterial hypertension	346 (65.4%)	239 (71.3%)	>0.05
Smoking	328 (62%)	186 (55.5%)	<0.05
Diabetes mellitus	60 (11.3%)	40 (11.7%)	>0.05
Hypercholesterolemia	342 (64.7%)	201 (60.0%)	>0.05
History of MI	78 (14.7%)	65 (19.4%)	>0.05
History of angina	163 (30.9%)	94 (28.1%)	>0.05
Ischemic Heart Disease onset	288 (54.4%)	176 (52.5%)	>0.05
Systemic thrombolytic therapy	100 (18.9%)	41(12.2%)	<0.05
LVEF, %	52.6±12.2	49±12.9	>0.05
Acute cardiac aneurism	86 (16.2%)	67 (20.0 %)	>0.05
Time from disease onset to therapy initiation up to 24 hours:	372 (70.3%)	245 (73.1%)	>0.05
a) < 6 hours	209 (39.5%)	125 (37.3%)	>0.05
b) 6-24 hours	163 (30.8%)	120 (35.8%)	>0.05
> 24 hours	157 (29.7%)	90 (26.9%)	>0.05

went urgent coronary angiography, and in case of stenotic or occlusive lesion of the coronary arteries the endovascular procedure of blood flow restoration in the infarct-related artery (IRA) was performed (fig. 1)

ECG and cardiovascular vital signs (blood pressure, heart rate, respiratory rate, pulse oxymetry) monitoring were performed in all MI patients.

After the stabilization the patients were transferred to the myocardial infarction department for

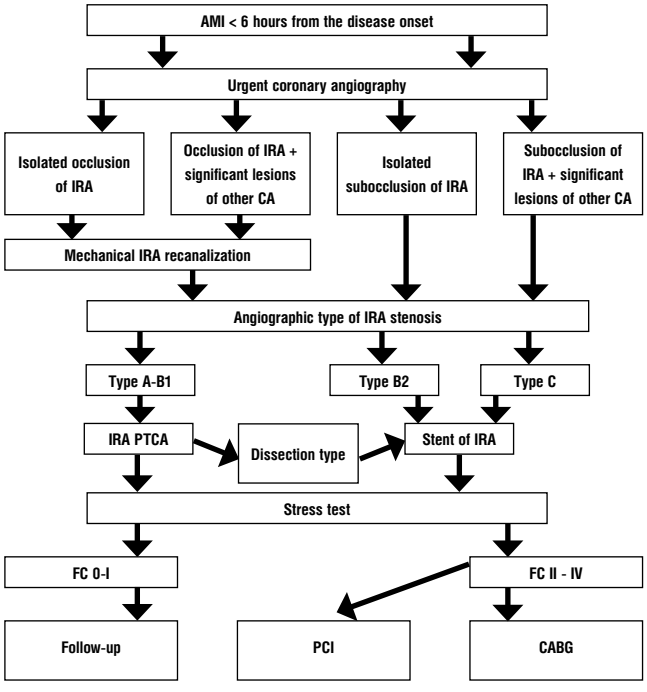

Figure 1 . Algorithm of treatment within the first hours of AMI.

Table 2. Main groups of medicaments prescribed to the patients from the groups of study during in-hospital period.

Medicaments	Endovascular treatment (n=529)	Conservative treatment (n=335)	p
Anticoagulants (heparin)	529 (100%)	335 (100%)	-
Antiplatelet agents	529 (100%)	335 (100%)	-
Nitrates	529 (100%)	335 (100%)	-
β – blockers	464 (87.7%)	292 (87.2%)	p>0.05
ACE inhibitors	391 (73.9 %)	252 (75.2%)	p>0.05
Diuretics	162 (30.6%)	112 (33.4%)	p<0.05
Inotropic agents	59 (11.2%)	53 (15.8%)	p<0.05
Calcium antagonists	165 (31.2%)	120 (33.6%)	p<0.05
Antiarrhythmic agents	34 (6.4%)	25 (7.5%)	p<0.001
Glycosides	38 (7.2%)	32 (9.6%)	p<0.05

further treatment and examination. As mentioned above, the patients from group 2 had no diagnostic and therapeutic procedures. They received standard conservative treatment (Table 2).

Statistical processing of the study results was performed using standard non-parametric statistical methods: Mann-Whitney test for comparing means, Spearmen correlation analysis (the differences were considered to be significant at $p < 0.05$, which corresponds to 95% CI according to Student table). The Fisher's exact test was used for statistical analysis with small number of cases.

STUDY RESULTS AND DISCUSSION

In group 1 immediate angiographical success of percutaneous interventions (PCI) (residual stenosis up to 30% in patients with PTCA and up to 20% in case of stenting, absence of type C-F dissection and distal embolization, antegrade blood flow restoration to TIMI 2-3) was high and amounted to 92.4% (489 patients). Among the complications related directly to PCI, in 21 cases (4,0%) thrombosis / reocclusion of the IRA was noted: in 1 case (0,2%) it led to the death of patient, in 8 cases (1,5%) – to the development of non-fatal recurrent MI. In another 12 patients (2,2%) with protracted angina attack and subocclusion of the IRA no signs of myocardial damage were revealed. All 20 (3,8%) patients with thrombosis of the IRA and 9 (1,7%) patients with clinical picture of unstable angina and threatening dissection of the vessel after primary angioplasty underwent successful repeated emergency PCIs with the restoration of antegrade blood flow TIMI 3 and subsequent non-complicated course of the disease. In 11 (2,1%) cases stenting of the IRA was accompanied by distal embolization (Table 3).

Clinical results of the study were evaluated on the base of the data on mortality, disease recurrence, MI, postinfarction angina, progressing circulatory insufficiency and cerebral stroke. The information concerning the in-hospital course of the disease is shown in Table 4.

Table 3. Complications and urgent PCI in immediate postoperative period.

Parameters	Group 1 (n=529)
Unsuccessful effort of mechanical recanalization	20 (7.1%)
Distal embolization	11 (2.1%)
Thrombosis/reocclusion of IRA (total)	21 (4.0%)
Non-fatal recurrent MI	8 (1.5%)
Prolonged angina attack (subocclusion of IRA)	12 (2.2%)
Death	1 (0.2%)
Unstable angina (threatening vessel dissection at angiography)	9 (1.7%)
Urgent repeated IRA transluminal angioplasty (total)	29 (5.5%)

Table 4. In-hospital results in the groups of study.

Parameters	Group 1 (n=529)	Group 2 (n=335)	p
Non-complicated course of the disease	436 (82.4%)	171 (51.0%)	0.0001
Complicated course of the disease:			
Angina attacks	22 (4.2%)	50 (15.0%)	0.001
Recurrence of MI (non-fatal)	(1.5%)	25 (7.5%)	0.04
HCirculatory insufficiency (Killip class I-III),	52 (9.8%)	50 (15.0%)	0.001
Other complications	26 (4.9%)	13 (3.9%)	0.6
Mortality:			
Total	11 (2.1%)	39 (11.6%)	0.001
Cardiac	7 (1.3%)	35 (10.5%)	0.001

Table 5. Analysis of in-hospital mortality in the groups of study.

Parameter	GROUP 1 (n=529)		GROUP 2 (n=335)		P <0.05
	Group 1A <24 hour (n=372)	Group 1B 24 hours - 21 days (n=157)	Group 2 A <24 hour (n=245)	Group 2B 24 hours - 21 days (n=90)	
Survival	518 (97.9%)		296 (88.3%)		For Gr.1 – Gr. 2
Mortality (general)	11 (2.1%)		39 (11.6%)		For Gr.1 – Gr. 2
	10 (2.7%)	1 (0.6%)	34 (13.9%)	5 (5.5%)	For 1A – 2A For 1B – 2B
Mortality (cardiac)	7 (1.3%)		35 (10.5%)		For Gr.1 – Gr. 2
	6 (1.6%)	1 (0.6%)	30 (12.2%)	5 (5.5%)	For 1A – 2A For 1B – 2B
Causes of death:					
- cardiogenic shock	1(2.0%)		10 (20.0%)		For Gr. 1-2
- Myocardial wall rupture	2(4.0%)		12 (24.0%)		For Gr. 1-2
- circulatory insufficiency (Killip class II-III)	2(4.0%)		9 (18.0%)		NS
- Ventricular fibrillation	1(2.0%)		4 (8.0%)		NS
- Acute coronary failure as a result of stent thrombosis / occlusion of the IRA	1(2.0%)		-		-

Uncomplicated clinical course of disease (without lethal cases, recurrent infarction, early post-MI angina reappearance, circulatory failure progression, acute cerebral circulation disorders, pulmonary embolism) was observed in 82.4% (432) patients of group 1 and in 51.0% (171) patients of group 2 (p<0.05).

In group 2, recurrent non-fatal myocardial infarction was seen in 7.5% (25) of patients, 15.0% (50) of patients had angina recurrence, 18.0% (9) of patients died from increasing circulatory failure and after CABG.

Thus, the use of PCI in AMI patients allowed for a significant increase of clinical success of treatment: from 51.0% with only conservative medical therapy to 82.4% with additional endovascular treatment.

Among non-cardiac complications in the groups of study we have noted: pulmonary artery embolism (PAE) – in 0.2% (1) cases in group 1 versus 0.9% (3) cases in group 2, gastrointestinal bleeding (GIB) – in 1.3% (7) cases versus 1.2% (4) in group 2, ischemic or hemorrhagic stroke – 0.6% (3) in group 1 versus 1.8% (6) in group 2.

In general, at in-hospital stage 50 (5.8%) out of 864 AMI patients died: in 4.8% (42) of cases the cause of death was cardiac and in 0.9% (8) of cases - non cardiac. The analysis of fatal outcomes at in-hospital stage in groups of endovascular and medical treatment is presented in Table 5.

Significantly higher mortality was observed in group 2 – 11.6% of patients. In group 1 this index was 2.1% (P=0.0001).

Cardiac mortality in the group of endovascular treatment also was significantly lower than in another group - 1.3% versus 10.5% (35) (p=0.0001). This difference was maintained both in patients hospitalized within the first 24 hours after the onset of the disease - 1.6% versus 12.2%, and in patients hospitalized in later terms - 0.6% versus 5.5%, respectively (p<0.05).

The main causes of in-hospital cardiac mortality were: cardiogenic shock – 2.0% (1) of cases in group 1 versus 20.0% (10) of cases in group 2, myocardium rupture with subsuquent cardiac tamponade – 4.0% (2) of cases in group 1 versus 24.0% (12) in group 2, cardiac failure refractory to treatment – 4.0% (2) of cases in group 1 versus 18% (9) of cases in group 2, complex rhythm and conduction disturbances refractory to cardioversion and pacing – 2.0% (1) in group 1 versus 8.0% (4) in group 2, and in the group of endovascular treatment 2.0% (1) of IRA stent/occlusion thrombosis after unsuccessful EVT effort.

In order to detect the factors that can affect the outcome of the disease in patients with AMI at in-hospital stage, we performed correlation -statistical analysis of clinical, laboratory and historical data of these patients. Such variables as age, sex, arterial hypertension, diabetes mellitus, history of MI, localization of lesion, presence of early post-infarction angina, recurrent MI, methods of treatment used (medical and endovascular) were analyzed with consideration of the time of revascularization.

According to our data, elderly age and female sex are the factors influencing unfavourable outcome of the disease. In whole, the mortality among women was higher than among men, while in Group 2 this phenomenon was more pronounced. The mortality in Group 2 women was 15,4% (10 out of 65) and in men 10,7% (29 out of 270). At the same time in Group 1, the mortality in women was 1,4% (1 out of 70) and in men – 2,2% (10 out of 459)

(j<0,05). The increase of age was also accompanied by the increase of mortality. The highest mortality was noted among Group 2 patients over 60 years (27 patients – 54,0%). Patients with the history of myocardial infarction, that is, with postinfarction cardiosclerosis, had less favourable prognosis in terms of mortality . The mortality among patients with recurrent AMI was higher in both groups – 14%, while in patients with primary MI it was 4,2% (p<0,05). Herewith this trend was more evident in Group2 – 21,5% versus 7,7% in Group 1 (p<0,05).

The probability of death also increases in patients with anterior wall infarction (54% of all lethal cases).

Functional state of the left ventricle plays a crucial role in the survival of AMI patients. Thus, any patient from both groups with 1st degree LV insufficiency was not dead, while the mortality in patients with 2nd, 3rd and 4th degrees of LV insufficiency was 6% in Group 1 and 38% in Group 2 (p<0,05).

One has to emphasize, that the mortality in cardiogenic shock was 33,3% in Group 1 and 100% in Group 2 (p<0,05).

The performed analysis revealed significant correlation of fatal outcome with the chosen method of treatment, the localization of myocardial infarction (anterior MI), the history of MI, low LV EF (<40%), cardiogenic shock.

In addition, the study revealed elderly age (> 60 years) and female sex to be predictors of cardiac mortality, but in the group of patients with medical treatment only. In general, this is consistent with the existing opinion that elderly age and female sex are the risk factors for complications development and in-hospital AMI mortality (7, 9, 12). However, in the group of endovascular treatment in this study there were no significant differences between patients aged < 65 years and > 65 years in the number of fatal cases and other cardiac complications, as well as between men and women.

In general, the analysis of hospital mortality demonstrated the higher efficacy of endovascular AMI treatment allowing to restore coronary blood flow in IRA and thereby to reduce cardinally the reperfusion time. Obtained data confirm the existing opinion that the reduction of the time for coronary blood flow restoration allows for maximal limitation of myocardial injury and thereby for the improvement of the immediate (hospital) prognosis (8, 10, 11, 13).

Thus, our study has convincingly shown that in-hospital course and the prognosis of the disease in AMI patients with similar clinical, anatomical and laboratory parameters seem more favourable after successful endovascular myocardial reperfusion, than after PTCA or stenting of the infarct-related artery. It concerns patients who received myocardial reperfusion within the first hours after the onset of the disease, as well as in later period of in-hospital treatment. In-hospital mortality in patients after endovascular myocardial reperfusion is fivefold lower than in patients who did not receive similar procedure. The indices of repeated AMI and in-hospital angina recurrence are also significantly lower after successful endovascular restoration of the blood flow in the infarct-related artery. The complications related to the procedure of endovascular myocardial reperfusion, as a rule, are rare and most of them can be easily corrected. This is true also for such serious complication as acute and subacute occlusion of the infarct-related artery after the procedure. Repeated procedures with successful reperfusion are feasible in the vast majority of patients. Our results allow to recommend the wide use of urgent endovascular procedures of myocardial reperfusion (balloon angioplasty and/or stenting of the infarct-related artery) in patients with acute myocardial infarction. This will not only provide an important medical effect, but also will be of huge social significance giving many citizens the possibility to return to their work and normal life style.

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Percutaneous Treatment of Bifurcation Stenosis with TABA^s Technique

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INTRODUCTION

The percutaneous treatment of bifurcation lesions is followed by an increased rate of restenosis particularly when both main vessel and side branch are stented (1 - 3). The current practice of interventional cardiology has been revolutionized by the advent of drug-eluting stents, which have been shown to reduce the incidence of major adverse cardiac events, such as death, MI, or target vessel revascularization, and the development of neointimal hyperplasia and restenosis (4 - 10).

However, the most effective strategy of treating bifurcation lesions is currently undefined. Recent data of bifurcation stenting using a T-technique with sirolimus-eluting stents, though being better than the previously used bare-metal stents, showed an overall restenosis rate of about 28% (11, 12). The vast majority of these, related to restenosis at the ostium of the side branch, which occurred in 22%, may reflect incomplete coverage of the side branch ostium thereby reducing the efficacy of the drug-eluting stent. Ensuring complete coverage of bifurcation lesions with a T-technique requires extreme precision in stent positioning, and importantly, the angle between the main vessel and side branch in the majority of bifurcations is significantly <90° making it difficult to attain an acceptable "T".

The crush technique is a strategy of bifurcation stenting that is technically and relatively easy to do, and by its nature, always ensures complete ostial coverage of the side branch (12 - 15). However, dislocation of the stent in the main vessel during the withdrawal of the balloon and the wire may occur. Metal condensation is another problem (16 - 18). On the starting point of the side branch, two stents combine and form a layer like a "wire filter" in the lumen (fig 1) increasing the risk of thrombogenesis. Thick metal layer, especially on the carina of the bifurcation, also may change the dynamical balance of the myocardium by altering the systolic and diastolic stretching of the heart. The following cases illustrate the TABA^s technique.

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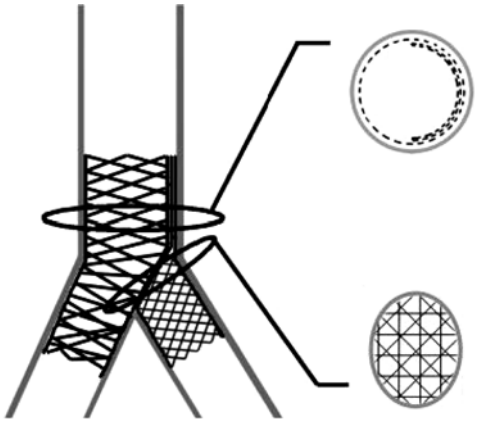


Figure 1.

CASE REPORT

CASE 1: TABA^s technique

A 70-year old man was admitted to the hospital with stable angina class 3B and known to have coronary artery disease with a previous history of two MI. Coronary angiography demonstrated significant multivessel disease with a severe stenosis of the right coronary artery, a mildly occluded circumflex artery, and a subtotal stenosis of the LAD just after the separation of the first diagonal branch (D1). The D1 also had a severe ostial disease (fig 2).

LAD and the first large diagonal branch were treated with bifurcation stenting using the TABA^s technique.

The patient has been taken to PCI for treatment of culprit lesion. The first guide catheter is inserted into one of the bifurcation sides (fig 3.1). Stent is deployed in the main branch (fig 3.2, fig 3.3). The other guidewire is inserted into the other branch of

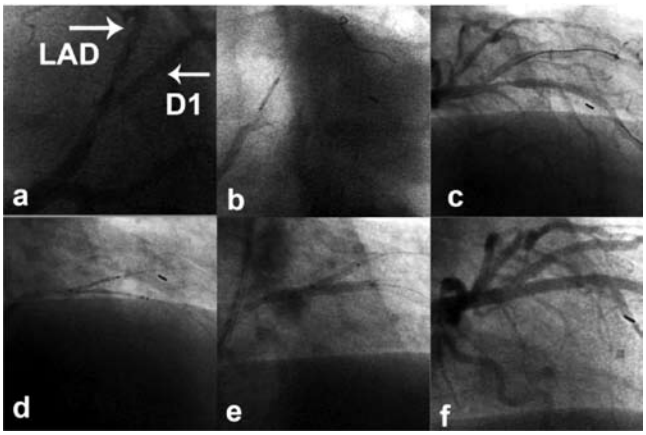
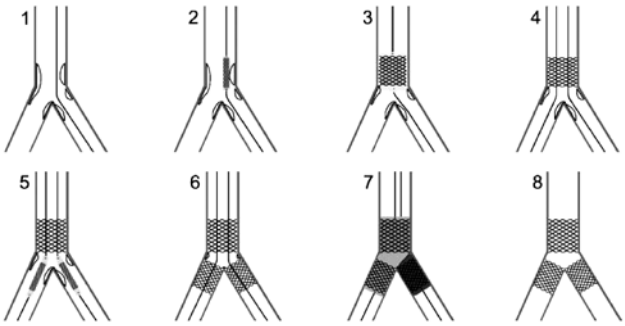


Figure 2.



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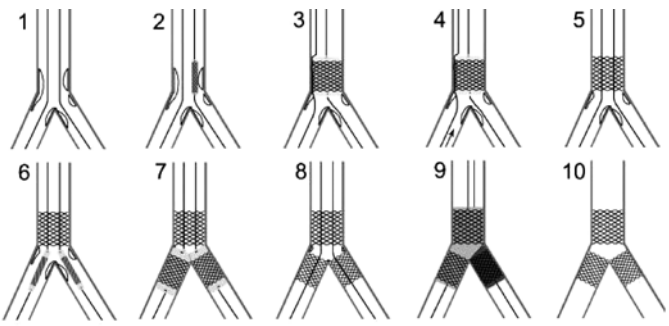


Figure 4.

the bifurcation (fig 3.4). The stents are deployed in both sides at the same time (fig 3.5, fig 3.6). Then a long balloon is inserted into the main + one side branch, also one balloon is inserted into the left side branch. Both balloons are inflated covering all the stents (fig 3.7).

The patient was discharged from the hospital the following day and at 3 months he was free from angina.

CASE 2: The Modified TABA^s

A 62-year old man was admitted to the hospital with unstable angina and presented with ST elevations on anterolateral leads. The following angiography revealed mild stenosis on circumflex artery, tortuous and severely narrowed lumen on bifurcation (D1) of LAD. He has uncontrolled hypertension and cholesterol.

First two guidewires are positioned into the both branches of the bifurcation (fig 4.1). By using one of the guidewires the CoStar stent (Conor systems inc) 3.5x10 mm is implanted into the main branch (fig 4.2, fig 4.3). The guidewire (the one, not used to deploy the stent) is pulled up (fig 4.4) and then moved ahead through the stent (fig 4.5). Then using the guidewires the CoStar (Conor systems inc) 3.0x16 and 3.0x16 mm stents are deployed to the branch vessels (fig 4.6). Two side branch stents are inflated at the same time (fig 4.7). Then a long balloon catheter (a longer balloon than the others) is inserted from one branch containing the main branch and one side branch (fig 4.8). The remaining one side branch balloon and new inserted main + side balloon are inflated simultaneously to take the optimal result (fig 4.9). By TABA^s technique one stent does not override the other (fig 4.10). In this way, there is only one layer of stent seen on the surface of the vessel.

The reason for inserting both guidewires before deployment of the main branch stent is the following. Sometimes while inflating the main branch due to the stretching or pushing effects of the main branch stent the side branches, that are narrow, may collapse and the lumen may be closed. If the closure of this lumen occurs due to the deployment of the main branch stent, we can run a secondary guidewire with the help of the side branch guidewire that has been inserted before.

The patient was discharged from the hospital the following day and at 3 months he was free from angina.

CASE 3: The Modified TABA^s

A 68-year old man with stable angina pectoris class 3A was admitted to the hospital with chest pain on effort. On ECG depressed ST waves have been seen on lateral leads.

Coronary angiogram revealed multiple mild lesions. Severe lesion on main branch and LAD is seen on bifurcation area (fig 5).

Patient underwent PCI for treatment. Due to the fact that the culprit lesion is on the main branch and a severe one, the first balloon dilatation is applied to the main branch (fig 6.2, fig 6.3). Then stenting is done as the mentioned TABA^s technique (in case 1).

TABAs technique may also be applied by overriding the stents in huge lesions on carina. The first guidewire is inserted into the side branch (fig 7.1). The main branch is stented (fig 7.2) and then side branches are stented (fig 7.3); the difference from the classical TABA^s technique is that the side stents are overridden on main stent and the whole lesion is covered by stents. Disadvantage of this technique is the occurrence of metal density in the lumen of the artery.

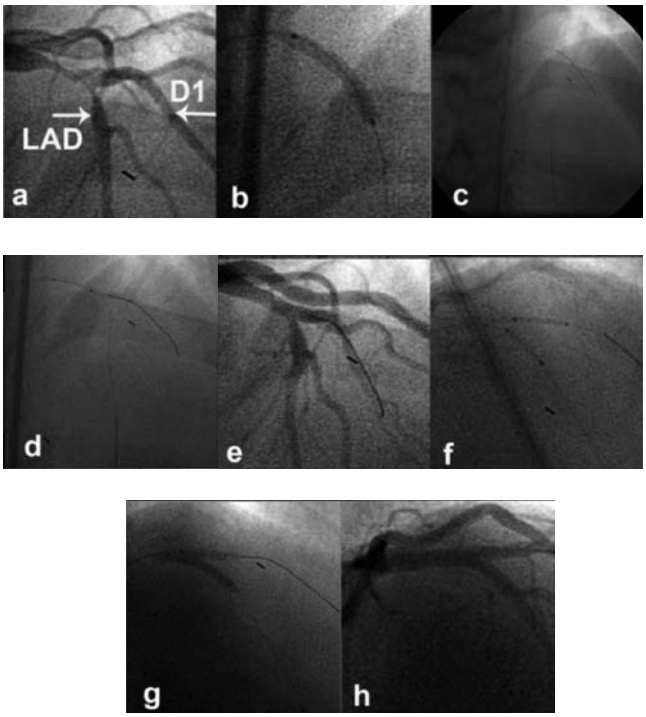
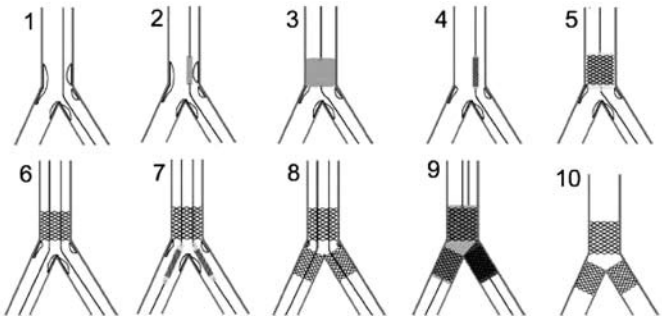


Figure 5.



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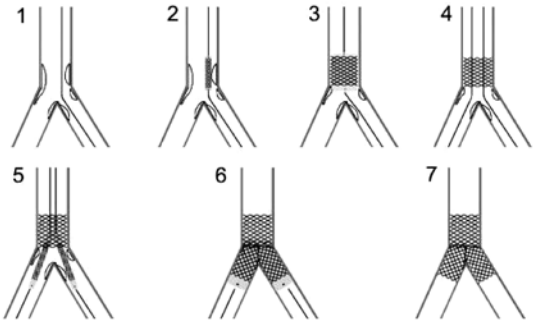

Figure 7.

CONCLUSION

In this case TABAs technique is described for development of bifurcation lesions in coronary arteries which are more difficult to treat than a linear arterial lesion. There were initial concerns regarding the potential for stent thrombosis particularly because of the high metal density at the carina for other techniques such as crush and T-technique (12, 14). This technique potentially prevents the occurrence of metal density at the carina (fig 8) and may decrease the major thrombotic symptoms such as MI, cardiogenic shock (12, 19). As far as the long-term results and rates of restenosis are concerned, the available data are still preliminary.

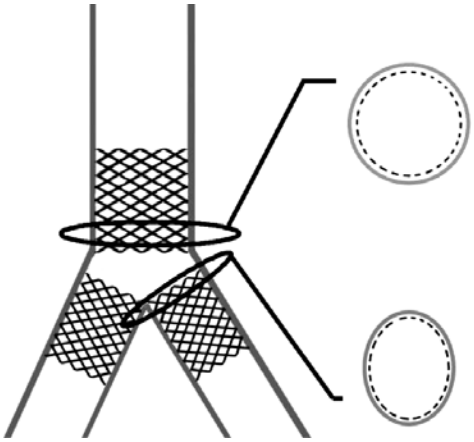

Figure 8.

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Influence of Coronary Stenting on Stunned Myocardium in Acute Coronary Syndrome with ST Elevation

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Restoration of adequate blood flow through the coronary arteries and sustained maintenance of tissue perfusion are the most important for ACS patients with ST elevation in whom complete coronary thrombotic occlusion is observed in 95% cases. It is known that urgent coronary recanalization allows to decrease myocardial necrosis area while preserving functional capability of the myocardium. Restoration of adequate blood flow through the ischemic area of the myocardium is absolutely necessary to preserve the tissue viability. Contractile dysfunction may be observed even after relatively short-term myocardial ischemia in spite of coronary blood flow restoration and absence of tissue necrosis. This phenomenon is known as stunned myocardium.

Postischemic myocardial dysfunction was first described in 1975 by G.R. Heyndrickx's research group after short-term coronary occlusion followed by reperfusion in experimental dogs (1). Introduction of such reperfusion strategies as thrombolysis and transluminal balloon angioplasty (TBA) has shown the role of postischemic dysfunction phenomenon in acute coronary syndrome. The clinical data suggest that the stunned myocardium is the main reason for heart failure in early ACS period and often is the cause of fatal outcomes. However, the mechanisms of myocardial dysfunction ar not fully understood.

In this study we tried to show the severity of stunned myocardium events in ACS with ST elevation and resolution of myocardial dysfunction over time after stenting of infarct-related coronary artery. For this purpose we have studied the time course of structural and functional parameters of the left ventricle (LV) in ACS patients with ST elevation prior to and after stenting of event-related coronary artery with determination of factors influencing on the degree and rate of restoration of LV contractile function.

MATERIAL AND METHODS OF THE STUDY

One hundred and fifty six (156) patients diagnosed with ST-elevation ACS were enrolled in this study. All patients were hospitalized for urgent indications at the Department of Cardiac Intensive Care of the Republican Scientific Centre of Emergency Care of the Ministry of Health Care of the Republic of Uzbekistan (Tashkent). Patients with cerebral vascular accident, recurrent myocardial infarction, atrial flutter, significant organ failure, cardiomyopathies as well as those admitted more than 24 hours after MI onset were not included in the study.

Selective coronarography and transluminal balloon angioplasty followed by coronary stenting were preformed at the cathlab of the Department of Angiography equipped with angiographic unit (Integris Allura FD 20, Philips) ECG monitoring was performed on Datex-Ohmeda (Finland) and Philips IntelliVue MP20 (Netherlands) devices.

Echocardiography (EchoCG) was performed on Siemens-Sonoline-Omnia device equipped with 4.0 MHz electronic transducers using standard technique in compliance with Guidelines of American Society of Echocardiography on Days 1, 3 and 7. In B-mode LV end diastolic volume (EDV) (ml), LV end-systolic volume (ESV) (ml), and ejection fraction (EF) (%) were calculated using "area-length" method.

To evaluate the regional contractility of LV the 15-segment model of LV division by Otto C.M., Pearlman A.S. (2) and the regional contractility impairment index (RCII) were used. The contractility of each segment was assessed using 5-point scale: normokinesis – 1 point, insignificant hypokinesis - 2 points, significant hypokinesis – 3 points, akinesis – 4 points and dyskinesis – 5 points. RCII was calculated by formula: RCII = TS/15, where TS is a total score for all 15 LV segments.

Prior to endovascular procedure heparin was administered intravenously at a dose of100 IU/kg body weight and antiplatelet drugs were prescribed - aspirin (325 mg) and clopidogrel (300 mg loading dose followed by 75 mg daily dose).

All patients enrolled in the study were treated in compliance with the Guidelines of American Heart Association and American College of Cardiology (2007) including anticoagulants, antiplatelet medications, beta-blockers, nitrates, and analgesics.

STATISTICS

Statistical processing of the data obtained from this study was performed on personal computer using electronic tables (EXCEL 7.0 for Windows XP). All values in the table are presented as M±SD, where M = mean, SD = standard deviation; consistency of numerical data with normal distribution law was assessed with Kolmogorov-Smirnov test. Alternative hypothesis with significance level no less than 95% (p=0.05) was used as statistical hypothesis.

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RESULTS OF THE STUDY

Clinical characteristics of patients enrolled in the study are presented in Table 1.

Table 1. Clinical characteristics of patients.

Parameter	Number of patients	
	Abs.	%
Total number of patients	156	100
Age, years (M±SD)	53.9±9.3	
Gender, men	136	88.5
History of angina	87	55.7
Arterial hypertension	65	41.6
Diabetes mellitus	33	21.1
Smoking	123	78.8
Hypercholesterolemia	120	76.9

Mean age of patients was 53.9±9.3 years. Time from pain onset to admission to the clinic ("symptom-door") was 3.2±2.7 hours, "symptom-balloon" time was 4.8±2.5 hours.

According to the results of diagnostic angiography 58 patients (37.2%) had right coronary artery lesion and 98 patients (62.8%) had the left anterior descending artery lesion; among these 128 patients (82%) had infarct-related coronary artery thrombosis with TIMI-0 blood flow, and 28 patients (18%) had TIMI-I blood flow. TBA followed by coronary stenting was performed by ad-hoc method immediately after diagnostic coronarography. After preliminary recanalization and predilatation, all 156 patients (100%) underwent primary coronary angioplasty with stenting of infarct-related coronary artery. TIMI-III blood flow was achieved in all patients and residual stenosis was less than 10%, which is an angiographic criterion of successful procedure.

EchoCG revealed, on the average, normal values of LA and LV parameters in admitted patients, however, LV systolic function was decreased. EchoCG data are presented in Table 2. As early as by Day 3, significant improvement of LV systolic function was observed – LV EF increased from 48.87% up to 51.64% ($p<0.01$) and by Day 7 increased up to 54.72% ($p<0.001$). By Day 7 of observation, LV EDV decreased from 131.8 ml to 128.6 ml ($p<0.05$). RCII decreased significantly by 22.5% and 24.6% by Day 3 and 7 of observation, respectively. Diagrams 1-3 demonstrate the time course of studied parameters.

Table 2. Time course of EchoCG parameters in ST-elevation ACS patients after coronary stenting.

Parameter	Baseline	Day 3	Day 7
EDV, mL	131.8±25.2	130.7±23.7	128.6±21.5*
SV, mL	64.3±14.0	67.0±12.7	69.8±11.9*
EF, %	48.8±7.1	51.6±5.8**	54.7±4.1***
RCII, U	1.42±0.20	1.1±0.05***	1.07±0.05***

Note: The significance of the difference from baseline parameters: *p<0.05. **p<0.01. ***p<0.001

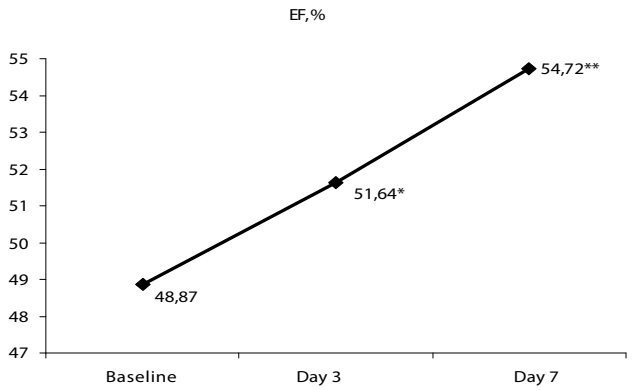

Diagram 1. Time course of LV EF in the study group.

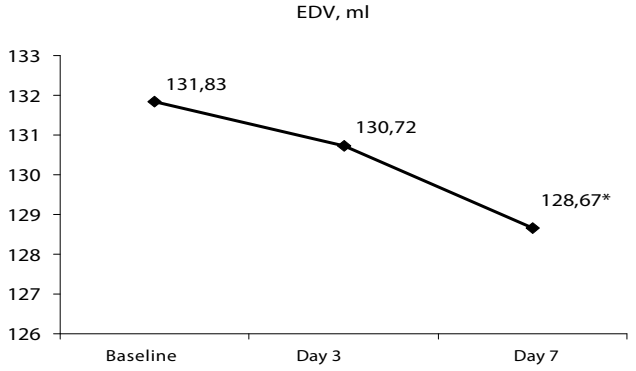

Diagram 2. Time course of LV EDV in the study group.

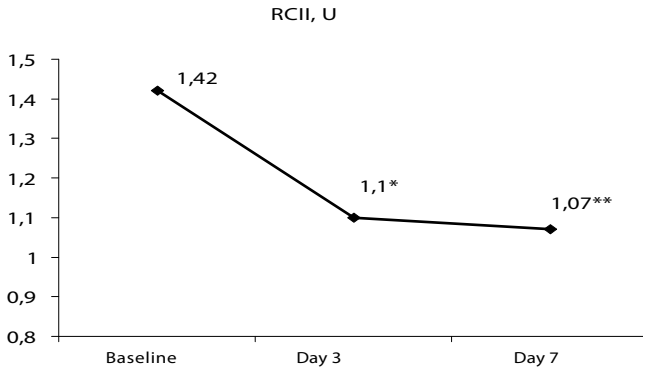

Diagram 3. Time course of RCII in the study group.

Thus, coronary stenting in ACS patients with ST elevation contributed to significant improvement of LV myocardial contractility already in the early stages of observation.

DISCUSSION

Researches in this area were advanced when reperfusion methods of MI treatment became available, which is evidenced by numerous literature data. Choi K.M. et al. (4) have established that following successful reperfusion therapy LV EF increases significantly not immediately after reperfusion but in several days only. Janardhanan R. et al. (5) have showed the improvement of LV systolic function in reperfusion area from the first weeks of MI. Ottervanger J. P. et al.(6) have revealed the delayed recovery of LV dys-

function after successful primary TBA in MI patients up to 6 months of observation. The authors have noted that the effect of recovery of myocardial contractility was minimal in patients with multivessel disease. The study of myocardial perfusion by EchoCG prior to and after reperfusion therapy in MI conducted by Sajad A. et al. revealed gradual improvement with sequential recovery of kinetics of hypo- and asynergic LV segments (7).

Myocardial reperfusion after short-term (less than 20 minutes) coronary occlusion is associated with slow recovery of its contractility in spite of rapid restoration of coronary blood flow up to the baseline values. The duration of the state of stunned myocardium is from several hours up to several days after ischemic episode. It was established that the rate of recovery of LV contractile function is higher in the subepicardial areas than in the subendocardium. This means that myocardial stunning is a non-homogeneous lesion, which is more prominent in the subendocardial areas. To date, myocardial stunning is defined as global disorder of mechanical properties of the heart, as both systolic and diastolic functions are inhibited in stunned myocardium.

When blood flow is restored after coronary occlusion with duration more than 20 30 minutes, the necrosis develops in the subendocardial areas, with a part of myocardium in subepicardial areas remaining viable. The subepicardial cardiomyocytes salvaged by reperfusion may require several days or even weeks to restore the contractile capability. Thus, urgent reperfusion in ACS with ST elevation leads to subendocardial infarction associated with stunned subepicardial myocardium (with irreversible and reversible dysfunction, respectively). Unfortunately, the event of stunned myocardium in myocardial infarction was not thoroughly studied due to numerous methodological problems.

Firstly, it is difficult to interpret the effect of therapy in this type of postischemic dysfunction because the myocardial area salvaged by reperfusion is a complex combination of necrosis areas in the subendocardium and stunned areas in the subepicardium, and relative proportions of these two tissues in different condition are very variable.

Secondly, subsequent expansion of infarction area and fixation of surviving myocytes by non-functional necrotic tissue and progressive replacement of necrotic myocardium with scar tissue possessing other structural and mechanic properties can develop (3).

Thus, as our study has shown, the restoration of normal coronary blood flow in ACS with ST elevation by stenting of infarct-related coronary artery as soon as possible after disease onset allows to significantly improve the heart pump function already since the first days of the disease due to more rapid recovery of stunned myocardium areas.

CONCLUSIONS:

1. TBA followed by stenting of infarct-related coronary artery in ACS with ST elevation is an effective method of pathogenic treatment.
2. Coronary stenting in ACS patients with ST elevation contributes to significantly improvement of LV systolic function.
3. Urgent restoration of adequate coronary blood flow in ACS with ST elevation leads to rapid restoration of LV regional contractility parameters due to stunned myocardium area reduction.

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Two-Stage Percutaneous Angioplasty in the Treatment of Chronic Renal Artery Occlusion

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Percutaneous interventions were performed in 13 patients with chronic occlusion of renal arteries. In all cases, stenoses more than 75% in the contralateral renal artery were revealed. Angioplasty and stenting of stenosed renal artery with simultaneous recanalization and balloon dilation of occluded vessel was performed as the first stage of revascularization. The second stage was control angiography on average in 36 hours; then stents were implanted in all patients provided that blood flow in renal artery was preserved with increased intensity of filling of the peripheral branches.

Recanalization was effective in 10 out of 13 patients (76.9%). There were no procedure-related complications at the site of reconstruction; mean in-hospital stay duration after stenting was 4.3±0.9 days.

The study results showed that percutaneous angioplasty is an effective and safe method for luminal restoration in chronic renal artery occlusion.

Keywords: atherosclerosis, occlusion, renal artery, renovascular hypertension, angioplasty, stent.

INTRODUCTION

Renal artery stenosis is a cause of increased blood pressure in 3% of patients with arterial hypertension (8). It is known that surgical revascularization remains a preferable method of treatment for these patients as compared to nephrectomy (1, 4, 6). Bypass surgery is recognized as an effective method for blood flow restoration in renal artery stenosis (2, 6). On the other hand, the complication rate of open surgery can achieve 5.3% (1). The development of methods of percutaneous renal revascularization allowed to reduce this value up to 2.0 % (1). Nevertheless, the efficacy and safety of percutaneous revascularization in chronic renal artery occlusion are not studied because of the limited number of observations (5).

MATERIAL AND METHODS

In the period from November 2006 till April 2008, 13 patients (7 women and 6 men) aged from 46 to 79 years (mean age 60.3±9.2 years) with chronic renal artery occlusion underwent percutaneous intervention. Contralateral renal artery stenosis was revealed in all patients. Concomitant coronary artery lesions were observed in 7 (50.0%), and carotid artery lesions – in 4 (28.5%) cases, respectively. Longitudinal renal dimensions assessed by ultrasonography ranged from 5.0 to 9.3 cm (mean 8.0±1.4 cm). Prior to revascularization, mean plasma creatinine level was 0.199±0.109 (ranged from 0.109 to 0.4) mmol/l, and mean systolic blood pressure was 171.2±56.7 mmHg.

Angioplasty and stenting of stenotic renal artery with simultaneous recanalization and balloon dilatation of occluded vessel was performed as a first stage of revascularization. The second stage was control angiography on average in 36 hours; then stents were implanted in all patients provided that blood flow in renal artery was preserved with increased intensity of filling of the peripheral branches.

Renal artery recanalization was performed using transport catheters - 8F introducers (Cordis, USA), 0.014'' guidewires (BMW, Cross-It–XT, Guidant, USA) and 0,035'' Glidewire (Terumo, Japan). Dilation was performed using Amiio balloon catheters (Cordis, USA), and Palmaz Blue, Genesis (Cordis, USA) and HercuLink Plus (Guidant, USA) stents. All patients were infused heparin 5.000 IU during the procedure and up to 30.000 IU during the first postoperative day under control of activated partial thromboplastin time (APTT). Plavix (clopidogrel) 75 mg/day was prescribed 48 hours prior to intervention.

RESULTS

Renal artery recanalization was effective in 10 out of 13 patients (76.9%). Delayed control angiography showed that vessel patency at the site of reconstruction was preserved in all cases, and residual luminal stenosis ranged from 60% to 80% (on average 70±7.0%) (Fig. 1).

Following stent implantation, the optimal result was achieved in all cases and residual stenosis at the site of reconstruction was 13.0±4.0% (Fig. 2).

A surgical intervention caused by bleeding at the site of femoral artery puncture was performed in one female patient (7.7%) in the early postoperative period. No other complications were observed.

After revascularization, plasma creatinine levels ranged from 0.098 to 0.370 mmol/l (on average 0.172±0.086 mmol/l), and mean systolic blood pressure did not changed significantly in early terms. Mean in-hospital stay duration after reconstruction was 4.3±0.9 days.

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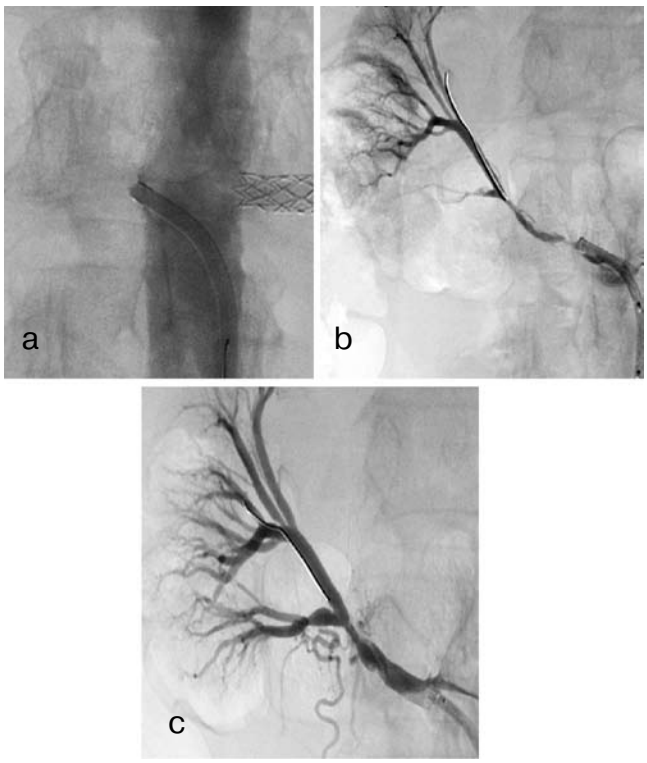

Figure 1. Female patient Sh., right renal arteriograms; a – occluded right renal artery; b (4th second) - after recanalization of occluded segment; c (4th second) – after balloon dilation ostial stenosis up to 70% with ill-defined contours and signs of intensive spasm at the site of renal artery bifurcation are observed, peripheral vessels are depleted.

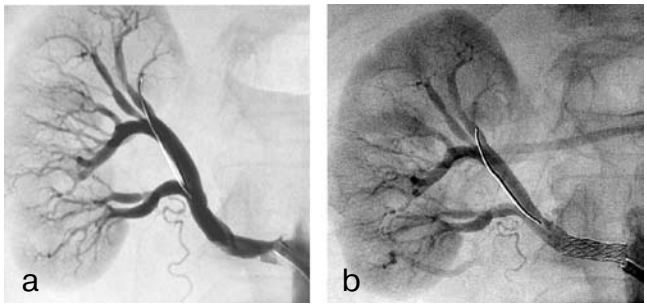

Figure 2. Female patient Sh, right renal arteriograms: (4th second) 24 hours after balloon dilation, a – there is no evidence of spasm, ostial stenosis has well-defined contours, peripheral vessels are in fair condition, b – there is an optimal result of reconstruction is seen following stent implantation.

DISCUSSION

It is known that blood flow restoration in renal artery occlusion is an independent predictor of improvement of long-term prognosis in patients with renovascular hypertension (1,6). However, targeted investigation of the results of percutaneous renal revascularization in this radiomorphological type of renal artery lesion was performed only by K. Sniderman K et al. (1982) in 7 patients.

The authors considered such possible complications as arterial perforation and dissection resulting in perinephric hematoma, embolization of distal arterial branches with fragments of atherosclerotic plaque to be disadvantages of intervention. In our study, no such complications were observed, which may be attributable to the use of modern tools compatible with 0.014'' guidewires.

Thus, as previous studies have shown, the efficacy of both surgical and percutaneous angioplasty was related to condition of peripheral renal vessels and renal dimensions (1, 5). It should be noted that after recanalization of an occlusion, the assessment of these parameters as well as artery condition at the site of intervention may be difficult. In this study, the final angiographic diagnostics of renal vessels was performed on the background of augmentation of antiaggregant therapy with Plavix 75 mg/day. Preservation of blood flow in the renal artery and increased intensity of peripheral vessels filling during delayed angiography allowed to assess the state of the renal arteries more objectively and to complete lumen restoration by stent implantation at the site of reconstruction.

CONCLUSION

The presented results of the study suggest that percutaneous interventions used as a revascularization method in chronic renal artery occlusion may be effective and safe. It should be emphasized that the number of patients with such radiomorphological type of lesion is scarce; and larger studies assessing long-term functional results of percutaneous interventions in this category of patients should be performed to determine the appropriateness of the use of this method in wide clinical practice.

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Comparison of Contrast Media Nephrotoxicity: Results of a Randomized Trial.

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Selective angiography and contrast computer tomography with contrast media (CM) enhancement are widely used in medical practice. Despite a significant progress achieved in the elaboration of CM, they still possess some unfavorable effects, including nephrotoxicity. Sometimes CM cause transient renal dysfunction, the so-called contrast-induced nephropathy (CIN), which can progress to chronic renal failure. The prevention of CIN remains a burning problem, as chronic renal failure worsens the prognosis in cardiovascular patients (1,2). It is known that endovascular interventions necessitate a greater volume of CM than diagnostic procedures, thus increasing the risk of CIN development.

We compared nephrotoxicity of isoosmolar and low osmolar contrast media used in interventional cardiology and angiology in order to determine the safest CM. We also evaluated the effectiveness of preventive measures and treatment of CIN, followed early and late prognosis of post-PCI patients who received different CM.

MATERIAL AND METHODS OF STUDY

300 patients admitted to the Department of Cardiovascular Surgery of CELT for the performance of endovascular interventions for coronary heart disease, peripheral, carotid and renal interventions, endovascular therapy of aortic aneurysm, were randomized.

Thirty-seven patients were excluded from the study: 7 patients who underwent repeated PCI during the same hospital stay; 6 patients – due to incomplete laboratory data; 6 patients who were unavailable for long-term follow-up. 18 patients who underwent diagnostic investigation the day before endovascular interventions, formed a separate comparison group.

263 patients were distributed into 4 groups depending of the CM used during the procedure: Iodixianol (Visipaque 320) - 60 patients; Iohexol (Omnipaque 300) - 70 patients; Ioversol (Optiray 300) - 67 patients and Iopromide (Ultravist 300) - 66 patients. 130 patients underwent angioplasty and stenting of the coronary arteries, 133 patients – angioplasty and stenting of the peripheral, carotid, renal arteries and the aorta.

CIN was determined as the increase of serum creatinine (SC) by 25% and more from the baseline within 48 hours after intraarterial administration of CM, in the absence of other evident causes of renal dysfunction.

Excluded from the study were patients with acute myocardial infarction, complicated by cardiogenic shock, patients on chronic hemodialysis, receiving non-steroid anti-inflammatory agents, cephalosporins, metformin, loop diuretics. Patients with anemia (baseline hemoglobin level < 100 g/l), those who underwent blood transfusion during in-hospital stay, pregnant women, as well as patients with severe associated diseases with life expectancy under 1 year were not included in the study.

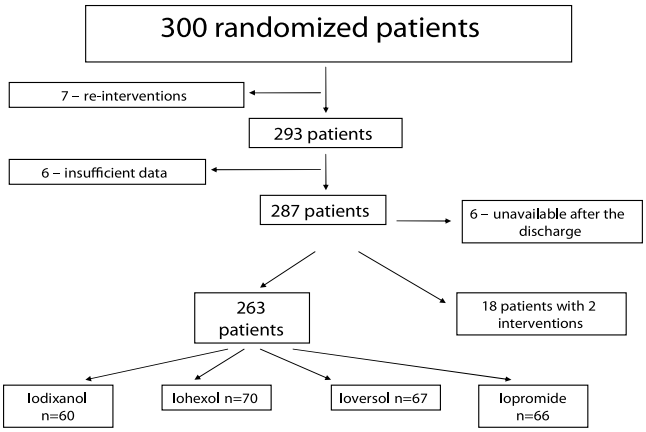

Figure 1. Patients' distribution after randomization.

Fasting SC level in venous blood was determined using an automatic biochemical analyzer. In order to study renal function creatinine clearance was calculated using Cockcroft-Gault equation.

$$ECC = \frac{(140 - age) \times Weight\ (kg) \times K}{Plasma\ creatinine\ (\mu mol/l)}$$

where ECC – estimated creatinine clearance, the constant K = 1,23 for men and 1,04 for women.

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Estimated creatinine level (ECC) above 60 ml/min was considered normal. Renal dysfunction (RD) was determined as ECC decrease below 60 ml/min.

In-hospital complications: acute renal failure with oligo- and anuria (diuresis < 20 ml/hour), acute myocardial infarction (the increase of CPK or MB CPK by over 3 times from the baseline, typical ECG changes), acute heart failure, hypotension – stable drop of systolic blood pressure < 90 mm Hg, necessitating inotropic support for over 1 hour, acute cerebrovascular accident with focal neurological symptoms, critical lower limb ischemia with ultrasonic and angiographic signs of decreased blood flow, any condition associated with the intervention which prolonged the hospital stay. The aneurysm or AV fistula formation, external or retroperitoneal bleeding, arterial thrombosis were considered the **complications at the access site**. «Major» and «minor» bleeding was assessed using TIMI scale.

Long-term complications: progressive RD in the form of SC level rise, chronic renal failure, necessity of hemodialysis, «major» and «minor» bleeding. The cases of repeated hospitalization for the main disease were also considered as complications.

Methods of CIN prevention and adjunctive treatment. Prior to endovascular procedure all patients were recommended to take fluids without restrictions. Two hours before the intervention IV infusion of isotonic solution of sodium chloride was started at a rate of 1 ml/kg/min, and was continued for 24 hours. In patients with congestive heart failure the rate of fluid administration was decreased twofold. In cases with baseline increase of creatinine level, 2400 mg/daily of N-acetyl cysteine (NAC) was administered the day before and after the intervention for CIN prevention. All patients received dual antiplatelet therapy with clopidogrel and aspirin.

Primary clinical end-point – frequency of CIN and progressive renal failure in the compared groups.

Secondary clinical end-points: mortality during the follow-up period, pooled cases of readmission, revascularization, bleeding, progressive renal dysfunction and cardiovascular mortality.

Statistical analysis. The data were analyzed using standard descriptive and analytical statistical methods. The description of the whole body of data was performed with the calculation of the means, standard deviations, standard errors, the minimum, the maximum, 95% confidence intervals, relative values. The data were analyzed using non-parametric statistical methods. The significance of the data differences in the groups was evaluated using χ^2 method, Kruskal-Wallis method, Wilcoxon test. The comparison of the item's value at different stages of dynamical follow-up was done using Friedman rank analysis of variance (Friedman ANOVA). The correlations between the items were studied using Spearman non-parametric rank correlation method. Different predictors of CIN were determined with the help of a non-linear logistic regression. Besides, we calculated the correlation of the likelihood and prognostic value of CIN development. Critical level of P value for the testing of statistical hypothesis in this study was determined as 0,05.

Results. The majority of our 263 patients were men – 209 (79,5%). The distribution of patients by sex was similar and not significantly different between the groups (χ^2 criterion = 1,11).

Most patients were admitted to our department with the leading clinical diagnosis of coronary heart artery disease (n=130) and chronic lower limb ischemia (n=122). The patients with CHD and peripheral artery disease were uniformly distributed between the study groups (Table 1). In isolated cases endovascular intervention s were performed in patients with acute myocardial infarction, aortic aneurysm and carotid stenosis. The main parameters, such as age, sex, associated disease, the frequency of diabetes mellitus, arterial hypertension, the rate of renal dysfunction prior to the intervention and the body mass index, were comparable between the groups (P>0,05). (Tables 1 and 2).

Table 1. Baseline clinical data.

Diagnosis	Groups			
	Iodixanol N=60	Iohexol N=70	Ioversol N=67	Iopromide N=66
CHD. angina				
Stable	21 (35%)	25 (36%)	21 (31%)	24 (36%)
Unstable	5 (8%)	7 (10%)	9 (13%)	7 (11%)
AMI:				
Q-wave	1 (1.5%)	2 (3%)	1 (1.5%)	1 (1.5%)
non Q-wave	1 (1.5%)	2 (3%)	1 (1.5%)	2 (3%)
CAI 2nd degree	6 (10%)	6 (8.5%)	9 (13%)	7 (11%)
3nd degree	10 (16%)	13 (18.5%)	10 (15%)	13 (20%)
4nd degree	11 (18%)	13 (18.5%)	14 (21%)	10 (15%)
Carotid stenoses	2 (3%)	1 (1.5%)	1 (1.5%)	1 (1.5%)
Renovascular AH	1 (1.5%)		1 (1.5%)	
Aortic aneurysm	2 (3%)	1 (1.5%)		1 (1.5%)
Non-significant differences between the groups CAI – chronic arterial insufficiency. AMI – acute myocardial infarction. AH – arterial hypertension.				

Table 2. Characteristics of patients in the groups of study.

Variable	Iodixanol N=60	Iohexol N=70	Ioversol N=67	Iopromide N=66
Age	59.9±11.1	61.4+9.8	61.5+11.3	58.35+11.1
BMI (kg/m^2)	28.8±4.5	32.4±5.5	29.1±4.9	29.0±4.0
Diabetes mellitus	20 (33%)	25 (35%)	23 (34%)	22 (33%)
AH	32 (53%)	35 (50%)	34 (51%)	36 (55%)
Baseline renal dysfunction, n (%)	22 (36.7%)	25 (35.7%)	23 (34.3%)	20 (30.3%)
Mean baseline SC level (μmol/l)	105.3±34.9	99.9±22.1	101.0±24.8	98.2±0.0

About one third of patients had type 2 diabetes mellitus, one half of patients had arterial hypertension (Table 2). Patients with baseline RD were evenly distributed between the groups. According to the analysis of variance using ANOVA test, this variable was not different between the groups (Table 3).

Table 3. Comparison of the groups on the base of the volume of CM used.

Amount of CM	Iodixanol N=60	Iohexol N=70	Ioversol N=67	Iopromide N=66
Mean volume (ml)	278.2+130.4	326.8+137.5	276.7+130.6	285.2+123.4
Volume in 95% CI (ml)	244.5	294.1*	244.8	254.8
Minimum (ml)	100	100	80	100
Maximum (ml)	950	800	700	650
Volume of CM / BMI	9.66	10.01	9.54	9.83

The differences between the groups do not reach statistical significance. *P=0,08
CI – confidence interval, CM – contrast medium, BMI – body mass index, kg/cm^2

In one half of patients - 133 out of 263 (50,5%) - the interventions were performed using the transradial approach, in the remaining 130 the femoral approach was used. The patients operated on from the femoral approach were uniformly distributed between the groups.

Immediate success rate after percutaneous coronary interventions was 98,5%. Immediate success rate after peripheral angioplasty was achieved in 100 out of 112 patients (89,2%). "Major" bleeding necessitating blood replacement occurred in 4 patients (2 cases in Iodixanol group and 1 case both in Iohexol and Iopromide groups). "Minor" bleeding was noted in 10 patients. There were 2 in-hospital deaths.

Frequency of CIN in the groups of study. At day 2 CIN was noted in 9 (3,4%) patients. At day 3 the increase of creatinine level by 25% from the baseline was noted in 14 (5,3%) patients. The same pattern was seen within each group. In total, during two days, the increase of SC level above normal values was seen in 18 out of 263 patients, that is, in 6,8%, while the increase by 25% from the baseline was seen in 17 (CIN frequency 6,4%).

The comparison between the groups revealed that at day 2 CIN was present in 3 (5,0%) patients in Iodixanol group, in 2 (2,9%) in Iohexol group, in 2 (3,0%) in Ioversol group and in 4 (5,9%) – in Iopromide group. No differences in the increase of creatinine level at day 2 were revealed between the groups (fig. 2). At day 3 CIN was present in 4 patients (6,6%) in Iodixanol group, in 3 (2,8%) - in Iohexol group, in 3 (4,5%) in Ioversol group and in 7 (10,6%) in Iopromide group. No difference was seen between the groups.

There were 90 patients with baseline renal dysfunction: 22 in Iodixanol group, 25 in Iohexol group, 23 in Ioversol group and 20 in Iopromide group. At day 3 CIN was noted in 6 of them (6,7%). There were 3 such cases in Iodixanol group3 (13,6%) , in Iohexol group – 2 (8,0%), 1 (4,3%) case – in Ioversol group and no cases in Iopromide group (fig. 3). The analysis did not reveal any difference in the frequency of CIN in such patients between the groups (Pearson χ^2 criterion 3,22; P = 0,36).

In 90 patients with baseline renal dysfunction mean ECC increased during 3 days in all groups and reached maximal value by the day 3. In total, the administration of contrast medium in the majority of patients did not worsen renal clearance.

In patients from Iodixanol and Ioversol groups with initially decreased creatinine clearance a statistically significant increase of predicted clearance occurred at day 2. At the same time these indices did not differ reliably between the groups (χ^2 criterion 1,6, Kruskell-Wallis method, P=0,66). The level of ECC in Ioversol group significantly increased in comparison with the baseline by the day 3 (fig. 4).

Taking into account that the tendencies were similar in all groups and there were no difference between them, we analyzed ECC dynamics in all patients. The comparison of all patients with initially decreased ECC, but with normal level of serum creatinine - this subgroup of patients can be provisionally designated as a subgroup with hidden renal dysfunction (in total 45 patients), – revealed a significant increase of ECC, that is, an "improvement" of renal dysfunction, in them by the day 3 (fig. 5).

The analysis of ECC changes in both groups revealed significant increase of this index only in the subgroup of 39 patients with moderately decreased ECC from 30 to 59 ml/min (Fig.6).

There were isolated cases of CIN among patients without RD. In Iodixanol group by the day 3 CIN was observed in 1 patient, in Iohexol group – in 2 and in Iopromide group – in 7 patients (Fig. 7).

As for estimated creatinine clearance, by the day 2 it was insignificantly decreased in comparison with the baseline in Iodixanol group, and by the day 3 there were no substantial changes. While the decrease of ECC by the day 2 was statistically reliable (P = 0,004), it was not significant when taken in absolute values (from 80,8 ml/min to 77,6 ml/min, table 4). By the day 3 ECC was virtually unchanged.

A statistically significant increase of ECC was seen in Ioversol group by the day 3 – from 86,8 ml/min to 87,6 ml/min (Table. 4). This made the difference between the Ioversol group and the remaining groups (the paired comparison with Iopromide and Iohexol groups revealed this difference to be statistically significant).

Fig. 8 displays ECC dynamics in all patients with RD and all patients with normal kidney function. One can see, that the predicted level of clearance in patients with baseline low indices statistically increase by the day 3 of the follow-up. By the same time the level of ECC in patients with baseline normal indices significantly decreased. The comparison of ECC dynamics using McNemar criterion dud not reveal the differences between the groups (fig. 8). However, as one can see, the values of ECC in the group with RD (renal dysfunction) are below 60 ml/min, while in the group with normal renal function they are higher than 60 ml/min.

RENAL FUNCTION IN PATIENTS UNDERGOING TWO INTERVENTIONS DURING THE SAME HOSPITAL STAY

Eighteen patients who were not included into the main groups and who underwent contrast investigation the day before their endovascular intervention, made a separate comparison group.

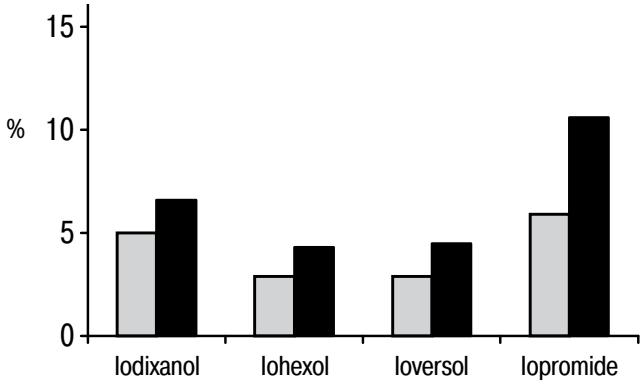

Figure 2. Frequency of CIN (%) at day 2 (light columns) and 3 (dark columns) in the groups of study.

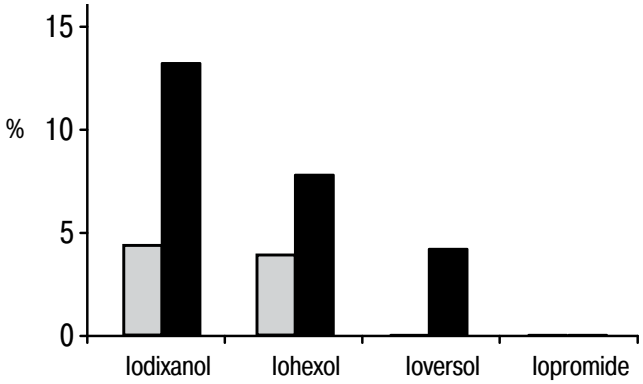

Figure 3. Frequency of CIN (%) in patients with renal dysfunction at day 2 (light columns) and 3 (dark columns).

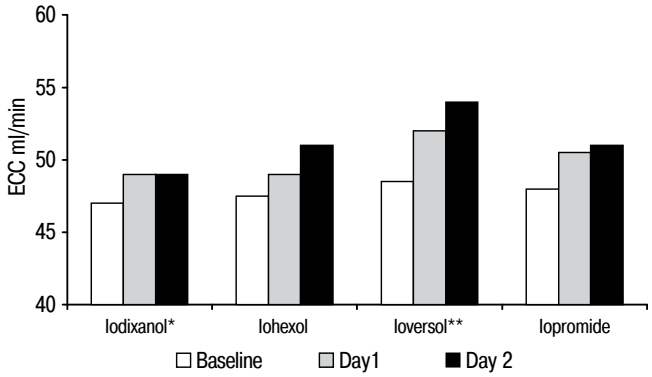

Figure 4. Dynamics of estimated creatinine clearance (ECC) in study groups. Statistically significant increase in the groups of Iodixanol* by the day 2 (P=0,03) and Ioversol ** by the days 2 (P=0,01) and 3 (P=0,03).

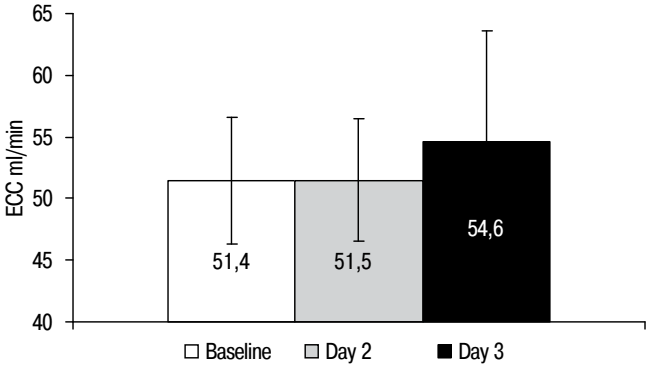

Figure 5. Dynamics of predicted estimated creatinine clearance (PCCECC) in patients with initially decreased clearance and normal creatinine level. Significant increase by the day 3 in comparison with the baseline (P=0,03).

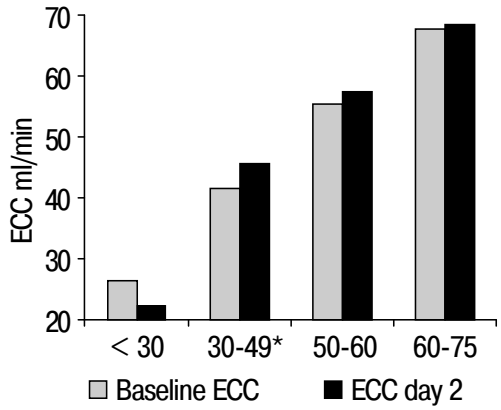

Figure 6. Estimated creatinine clearance changes (ECC) in subgroups of patients with different levels of renal function * Significant increase, P=0,001 (Wilcoxon test).

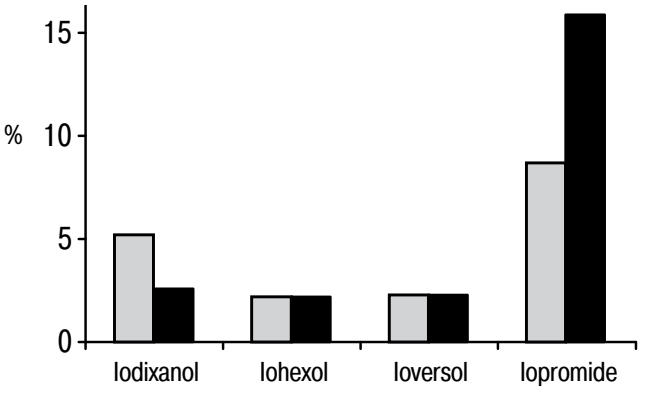

Figure 7. Frequency of CIN in patients with normal renal function at the days 2 and 3 (light and dark columns). Despite a higher frequency of CIN in Iopromide group, the difference with the remaining groups is not reliable..

Table 4. Dynamics of estimated creatinine clearance (ECC) at day 2 (ECC day 2) and 3 (ECC day 3).

Contrast medium (n)	Baseline ECC (ml/min)	ECC day 2 (ml/min)	ECC day 3 (ml/min)
Iodixanol (38)	87.8±4.2	84.3 ±3.8	83.4 ±4.0*
Iohexol (45)	82.8±2.4	79.6 ±2.1*	81.4 ±2.4
Ioversol (43)	86.8±3.6	85.1±3.6	87.6±4.0*
Iopromide (46)	88.9±3.1	86.2±3.0	85.2±3.3

* Significant change in comparison with the baseline PCCECC, P < 0,05.

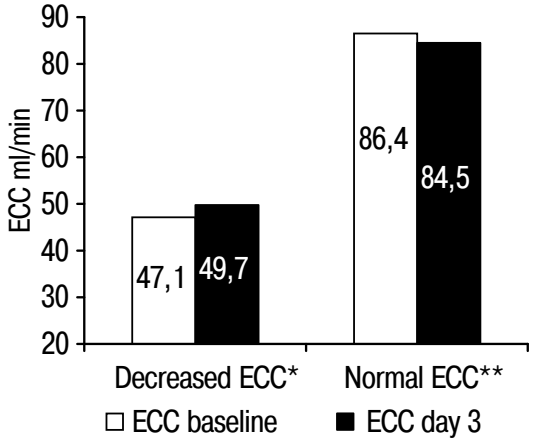

Figure 8. ECC dynamics in patients with decreased (left) and normal (ruight) clearance at baseline and at the day 3 (ECC 2). * P=0,017 ** P=0,046.

Clinical characteristics of these patients were similar to those of the main cohort of patients included into the groups of study. Seven patients from this group (35%) had diabetes mellitus, 9 (50%) had arterial hypertension, 5 (28%) patients had baseline renal dysfunction. Mean ECC in this group was 92,2±2,5 ml/min, mean SC level was 102,0±22,8 μmol/l. The difference between this group and the remaining patients consisted in the fact that CM was administered in them twice within 24 hours.

Prevention measures and their impact on the frequency of CIN. As mentioned above, hydration (IV administration of isotonic sodium chloride solution) was the universal method for CIN prevention in our study.

Patients with baseline increase of SC level received an additional infusion of NAC. The results of these two groups comparison are shown in Table 5.

Table 5. Changes in estimated creatinine clearance depending on the method of CIN prevention.

Group	Prevention	ECC increase after 1 day (ml/min)	ECC increase after 2 days (ml/min)
Iodixanol	Hydration +NAC	1.59	2.56*
	Hydration	-3.2	-3.9
Iohexol	Hydration +NAC	0.37	2.21
	Hydration	-2.1	-1
Ioversol	Hydration +NAC	3.14	5.46*
	Hydration	-0.7	3.1*
Iopromide	Hydration +NAC	2.26	1.36
	Hydration	-2.6	-3.3

*P < 0,05 as compared with the baseline.

As one can see from this table, when hydration was supplemented by NAC infusion, a clear trend of creatinine clearance increase was revealed, which was significant in Iodixanol and Ioversol groups. At the same time the use of hydration alone predominantly led to ECC decrease (negative differences), except for Ioversol group, where ECC increased.

IMPACT OF CIN ON THE OUTCOMES OF ENDOVASCULAR INTERVENTIONS

In-hospital clinical outcomes were not different between the groups. There was 1 case of acute renal failure in Iodixanol group requiring renal replacement therapy for 1 day, with kidneys' filtration function restoration within 1 week. Another patient from the same group died from multiorgan failure after repeated endovascular intervention performed within 1 day after the first one and a massive blood loss requiring transfusion. No in-hospital complications occurred in Iohexol group. One patient in Ioversol group died from acute cardiovascular failure, while no lethal outcomes were encountered in Iopromide group (fig. 9).

Within 1 month of the follow-up 1 patient from Iodixanol group was readmitted and underwent re-intervention, 1 patient from Iohexol group had control angiographic study, 1 patient from Ioversol group suffered from progressive chronic renal failure but did not require hemodialysis, and 1 patient from Iopromide group was readmitted for the recurrence of his main disease.

During 1 year follow-up there was 1 patient in Iodixanol group died from progressive renal failure necessitating hemodialysis. There were 2 cardiovascular deaths in Iohexol group. One patient in Ioversol group suffered from progressive chronic renal failure and died from gastrointestinal bleeding, and two patients in Iopromide group died from cardiovascular causes. There were no statistical differences in hard end points during the hospital stay and within 1 year after the interventions. Two patients from each group had to be readmitted for repeated interventions for the main disease (fig. 9).

One-month in-hospital and 12-month mortality was not statistically different between the groups. The total number of unfavorable outcomes was small and did not provide statistically significant differences between the groups of study.

PROGNOSTIC VALUE OF CIN

Multivariate analysis shows that in the presence of baseline SV level within the normal values, and ECC above 75 ml/min., the risk of CIN is minimal.

CIN was seen within two days after the intervention in 4 patients who later developed acute or chronic renal failure, however in the majority of patients with CIN (in total – 14) further course of the disease was uncomplicated. In this case, the prognostic value in the prediction of further deterioration of renal function can be calculated as:

$$4/4+14=4/18=22,2\%$$

The increase of SC level by over 50% from the baseline was noted in 2 out of 4 patients, who later developed acute or chronic renal failure. In this case the prognostic value of SC increase is high and equals:

$$2/(2+2)=2/4=50\%$$

The increase of SC level by over 40 μmol/l (0,45 mg/dl) is of even greater prognostic value. Chronic renal failure (necessitating hemodialysis) developed in 3 out of 4 patients in whom SC level was increased by over 40 μmol/l. The prognostic value of this index is equal to:

$$3/(1+3)=3/4=75\%.$$

According to logistic regression analysis, the increase of SC level by ⩾40 μmol/l was the most significant predictors of unfavorable outcome.

The risk of CIN depending on different predictors was also studied using non-linear regression analysis, which revealed an association between the risk factors and the frequency of CIN development. According to our data, the risk factors for CIN (in decreasing order of significance) were: baseline SC level above 170 μmol/l, ECC under 30 ml/min, CM volume over 500 ml, age >70 years and diabetes mellitus. Such risk factors as BMI <25, male sex, congestive heart failure, moderately decreased ECC (50-60 ml/min) were less significant.

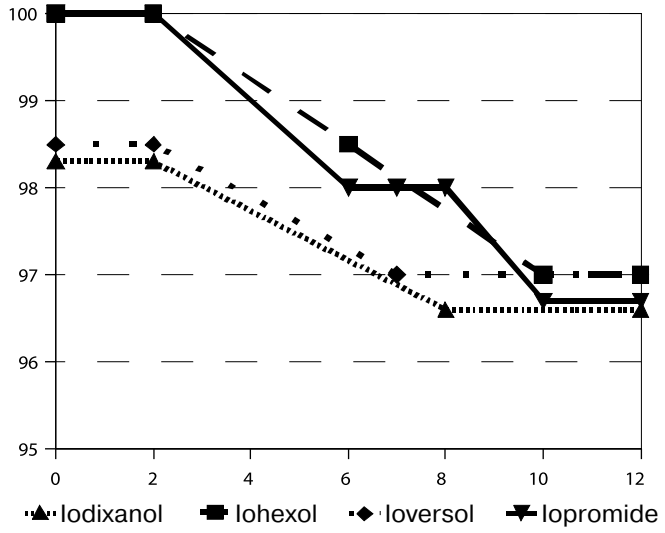

Figure 9. Survival (%) without complications in the groups of study within 12 months of the follow-up.

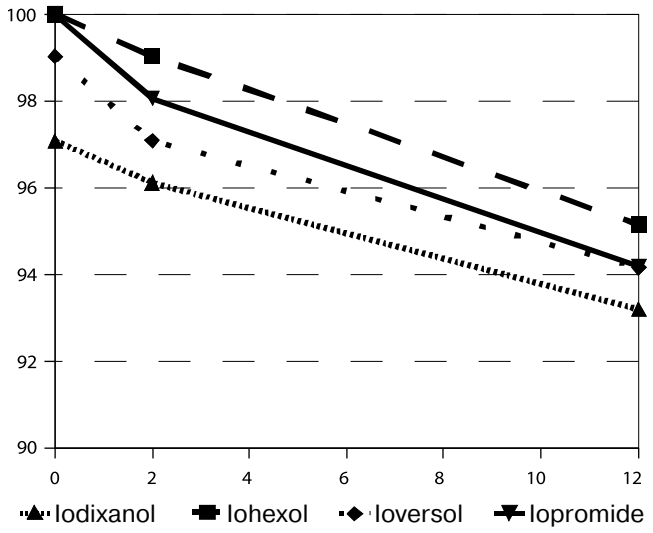

Figure 10. Survival, re-interventions and hemodialysis (%)in the groups of study within 12 months of the follow-up.

DISCUSSION

Due to wide spreading of contrast methods of diagnostics and treatment, their use in clinical practice and emergency care, inevitable aging of the population, the risk of CIN is steadily increasing (3-7).

According to our data, from the viewpoint of induced CIN the iso-osmolar CM Iodixanol has no advantages as compared with low-osmolar CM Iohexol, Ioversol and Iopromide, which, in general, is compatible with the conclusions of the majority of recent trials aimed at the comparison of these two types of CM (8), with the exception of early trials comparing Iodixanol with Iohexol, where the advantages of iso-osmolar CM had been shown (9).

Before endovascular intervention RD was present in less than one half of our patients. Besides, SC increase by ⩾25% from the baseline was considered as CIN criterion. Probably, our conclusions were influenced by the use of stricter criteria for CIN definition (SC increase by > 0.5 mmol/l), than those used in other trials (3, 10), the inclusion of patients not only with compromised renal function.

Our data contradict the existing opinion on inevitable transient deterioration of glomerular filtration rate in response to CM administration, especially in the presence of renal dysfunction (11,12,13). This contradiction can be explained by the fact that the majority of patients with RD in our study had moderately decreased ECC, and we have actively used hydration and high doses of NAC for a long time, while in other, especially early studies, no such attention was given to the prevention of CIN.

Besides, one has to note that the “improvement” of the renal function was relative, as mean values of ECC were still below 60 ml/min.

It is known that repeated administration of CM increases the risk of CIN and renal dysfunction (14-16). Our comparison did not reveal any case of CIN in this group of patients (CI for the frequencies in the groups included 0). Also, there were no differences in ECC dynamics and creatinine level between this group and other groups of study. Probably, more prolonged hydration in the group of re-interventions in comparison with the main groups of patients allowed to avoid CIN development.

Our data are compatible with other author’s conclusions on the effectiveness of NAC for CIN prevention (17-20). Probably, the use of NAC allowed to avoid ECC decrease in patients with compromised renal function, as the patients with all known risks for CIN development (advanced age, diabetes mellitus) prevailed in this group. The issue of the necessity of NAC use in all cases of CM administration remains open.

In general, in-hospital and long-term prognosis of our patients was favorable. Immediate and long-term outcomes of the disease in other trials, dealing with the prognosis, were les favorable (19-23). The possible causes for such differences were the inclusion of patients predominantly with renal dysfunction, almost exclusively with coronary heart disease, often with acute coronary syndrome, as well as different protocols used for CIN prevention in these trials.

CONCLUSION

According to our data, we concluded that the frequency of contrast-induced nephropathy does not depend of the use of modern iso-osmolar and low-osmolar contrast media– Iodixanol, Iohexol, Ioversol and Iopromide. In the presence of normal and moderately decreased renal function contrast-induced nephropathy develops in less than 10% cases. The use of Ioversol and Iodixanol in the majority of patients with moderate renal dysfunction does not lead to further deterioration of kidney function.

The increase of SC level by 25% from the baseline after endovascular intervention does not significantly influence the prognosis of cardiovascular patients, while the increase of SC level by 50% from the baseline of by 40 μmol/l after endovascular intervention is

a prognostically unfavorable sign and predicts with high probability the unfavorable events within 1 year after the intervention.

Simple and available methods for CIN prevention (adequate hydration and use of anti-oxydants) allow to avoid the deterioration of kidneys' function even in patients with baseline renal dysfunction and after the administration of high volumes of contrast media.

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Acute Kidney Injury after Percutaneous Coronary Interventions in Patients with Initially Impaired Glomerular Filtration Rate

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SUMMARY

In 1159 patients who underwent percutaneous coronary intervention (PCI) with implantation of bare metal stent or drug-eluting stent, the rate of acute renal failure (ARF) and the role of initially decreased renal function were evaluated. The initial renal function was evaluated using glomerular filtration rate (GFR according to MDRD formula). The patients` groups were formed by type of implanted stents and initial GFR (⩾ 60 ml/min/1,73м^2, from 30 to 60 ml/min/1,73м^2, less than 30 ml/min/1,73м^2). The prevention of contrast-induced ARF was performed in all patients with decreased GFR: hydration before and after angiography, nephrotoxic drugs restriction, N-acetylcysteine 600 mg/day orally. Only the nonionic contrast agent iodixanol was used in all patients. The direct PCI success was comparable in all groups. The rate of ARF increased significantly with GFR decreasing and was independent from type of implanted stents. The trend to increase in in-hospital mortality parallel to decrease of GFR did not differ significantly between groups. Thus, the initially decreased GFR is associated with increased risk of ARF without the significant increase of in-hospital mortality after elective PCI when performing the prevention of nephropathy.

Keywords: coronary heart disease (CHD), percutaneous coronary interventions (PCI), chronic kidney disease (CKD), glomerular filtration rate (GFR), acute renal failure (ARF).

INTRODUCTION

In recent years, the chronic kidney disease (CKD) have been spreading like epidemic (1). The chronic renal failure (CRF) is also observed in patients with CHD with increased rate (2). Previous studies showed that chronic kidney disease with decreased glomerular filtration rate (GFR) negatively influence the outcomes of percutaneous coronary interventions (PCI) (3, 4, 5). These data were obtained in the era of bare metal stents (BMS).

One of the dangerous PCI complications involving excretory system is an acute renal failure (ARF) which develops after administration of contrast media in the body (6, 7). The rate of ARF varies significantly depending on baseline patient condition and presence of nephropathy risk factors (2, 4). Due to introduction of new nonionic and less osmotic contrast media, which are more safe, and taking into consideration the risk factors and prophylaxis of complications, the incidence of contrast-induced ARF decreased from 15% to 7% since middle 90th (8). Nevertheless, contrast media remain the third most common cause of ARF development in hospitalized patients and comprise 11% of all ARF cases according to Nash et al. (7).

Introduction of drug-eluting stent (DES) into clinical practice of PCI significantly widened the frontiers of interventional cardiology (2). The use of DES led to significantly decreased incidence of adverse events and, primarily, the rate of repeated interventions (2). Meanwhile, in the modern practice of percutaneous coronary interventions, when drug-eluting stents are used in parallel to bare metal stents, the role of chronic kidney disease contrast-induced ARF remains underestimated.

Therefore, the purpose of this study was to compare the incidence of contrast induced ARF following the use of BMS and DES, as well as to evaluate the role of baseline renal function in development of post-interventional fatal and non-fatal in hospital complications.

MATERIAL AND METHODS

One thousand and one hundred fifty nine patients underwent PCI with implantation of one or more stent in 2004-2005 were enrolled in this study. In 2004, bare metal stents were implanted in 727 patients, and in 2005 drug-eluting stents (sirolimus and paclitaxel) were implanted in 432 patients. The patients with stable angina (II-IV class according to CCS classification) or unstable angina with negative biochemical cardiac markers were enrolled in this study, and

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condition all of patients was stabilized before angiography. Five hundred and fifty one patients suffered from chronic kidney disease, and 442 patients with CKD had moderate or severe decrease in glomerular filtration rate (GFR less than 60 ml/min/1.73 м^2), before stenting, i.e. they had CKD stage 3-4. Six hundred and eight patients suffered from CKD and were enrolled in control groups.

Patients with history of any revascularizations (percutaneous coronary intervention or open coronary artery bypass grafting) were not enrolled in the study: The patients with history of hemodialysis before stenting were also excluded from the study. All the patients were informed about the treatment methods and signed the informed consent for all types of interventions.

The recommendations K/DOQI (2002) were used in order to characterize the renal function (10). According to these recommendation the criteria of CKD were the following: a) renal impairment ⩾ 3 months with decreased GRF, or b) GFR < 60 ml/min/1,73 м^2 ⩾ 3 months with renal impairment or without it.

The clinically significant acute renal impairment after administration of contrast agent (acute renal failure, also called contrast-induced nephropathy) was defined as relative increase in serum creatinine level by more than 25% from baseline or absolute increase by more than 0.5 mg/dl from baseline within 48-72 hours after administration of contrast media in the body (11).

STATISTICAL CONSIDERATIONS

The study results were processed using the application programs patch BioStat (S.Glanz ©, USA 1999), Statistica for Windows 6.0 (StatSoft Inc., USA 2001).

In case of normal distribution the univariate analysis of variance (ANOVA) was used for primary comparison of data between groups using methods of multiple comparisons if significant differences were revealed. If normal distribution was not confirmed, the ordinal criteria Mann-Whitney or Kruskall-Wallis were used. The "χ2" criterion or Fisher's exact test were used for qualitative characteristics evaluation. The portions were compared using z-test with Yates correction or using Fisher's exact test. For all types of analysis the evaluation of obtained results representativeness was performed. p values less than 0.05 were considered as statistically significant.

CLINICAL AND ANGIOGRAPHIC CHARACTERISTIC OF PATIENTS

All patients were divided into 3 groups according to baseline degree of renal function impairment (of absence of renal function impairment). The patients were also divided according to the type of implanted stents (BMS or DES). The degree of renal function impairment was evaluated using glomerular filtration rate measured before angiography/PCI. The GFR was estimated using MDRD formula: the patients with GFR of more than 60 ml/min/1,73м^2 were included in the 1st group of normal or insignificantly decreased GFR (intact kidneys, CKD stages 1 and 2), the patients with GFR of 30-60 ml/min/1,73м^2 were included in the 2nd group of moderately decreased GFR (CKD stage 3), the patients with GFR of less than 30 ml/min/1,73м^2 were included in the 3rd group of severely decreased GFR (CKD stage 4).

In the 1st group including 737 patients with GFR of more than 60 ml/min/1,73м^2 there were 129 patients (17.5%) with CKD stage 1 and 2 (without decreased GFR). Main clinical parameters of patients are shown in Table 1.

More than a half of patients with decreased GFR (groups 2 and 3) had the increased blood cholesterol level (more than 5.2 mmol/l) and/or the increased blood level of low-density lipoproteids (more than 2.6 mmol/l). The 20% of patients with CKD suffered from diabetes mellitus and received the specific therapy orally or subcutaneous insulin. Arterial hypertension was diagnosed in 74-87% of patients with decreased GFR. The baseline rheological parameters in patients were within normal range.

Table 1. Baseline clinical characteristics of patients.

Parameter	Group 1 (n=737)	Group 2 (n=355)	Group 3 (n=67)	P
Renal function characteristic	GFR of 60 ml/min/1.73м^2	GFR of 30-60 ml/min/1.73м^2	GFR of less then 30 ml/min/1.73м^2	
Males	75%	73%	66%	0.04
Smokers	37%	45%	39%	0.03
CHF	10%	12%	15%	NS
Diabetes mellitus	12%	21%	28%	0.006
Arterial hypertension	58%	74%	87%	0.001
Hypercholesterolemia	39%	51%	58%	0.001
Prior MI	19%	33%	28%	0.009

In all patients with GFR of less then 60 ml/min/1.73m^2 the prevention of contrast-induced ARF was conducted before coronarography. The adequate hydration of patients (not less than 100 ml of liquid per hour) was performed 4 hours before angiography and during 24 hours after angiography, as well as the restriction of nephrotoxic drugs. The N-acetylcysteine at a dose 600 mg/day orally was also administered 48 hours before invasive investigation.

Only the nonionic contrast agent iodixanol was used in all patients, and we tried to reduce its quantity when possible. The total amount of contrast agent used for diagnostic coronarography and stenting did not exceed 350 ml for GFR 45-59 ml/min/1,73м^2, and did not exceed 250 ml for GFR less than 45 ml/min/1,73м^2. In all patients with GFR more than 60 ml/min/1,73м^2 (group 1) the total amount of contrast agent used for coronarography and stenting did not exceed 600 ml. In order to prevent ARF, coronary stenting was delayed in all patients with decreased GFR (less than 60 ml/min/1,73м^2 – groups 2 and 3) and performed within 3-5 days after coronarography, and in 540 of 737 patients from group 1 (with GFR

more than 60 ml/min/1,73м^2) the coronary stenting was performed as integrated procedure along with diagnostic coronarography.

The single-vessel lesion was observed in 43% of patients from group 1 with normal GFR, in 52% of patients from group 2 with GFR 30-59 ml/min/1,73м^2 and in 60% of patients from group 3 with GFR less than 30 ml/min/1,73м^2. The portion of three-vessel disease was the smallest - 21%, 16% and 13%, respectively (Table 2). The caliber of target arteries was the biggest in group 1 (with normal GFR) and the smallest in group 2 (with GFR 30-60 ml/min/1,73м^2). The portion of stenosis was the biggest in group 3 (with GFR less than 30 ml/min/1,73м^2). Main baseline angiographic values are shown in Table 2.

The median reference diameter in the affected area was bigger in group 1. The bifurcational stenoses occurred more often in group 2. Three-vessel disease occurred less often in group 3.

Table 2. Baseline angiographic characteristics of patients.

Parameter	Group 1 (n=737)	Group 2 (n=355)	Group 3 (n=67)	P
Single-vessel lesion	43%	52%	60%	0.02
Two-vessel lesion	36%	32%	27%	NS
Three-vessel lesion	21%	16%	13%	NS
Total amount of affected vessels	1309	582	103	-
Stenosis length. mm	15±4	14±5	13±5	NS
Reference diameter of the affected segment. mm	3.27±0.49	3.10±0.46	3.14±0.51	0.001
Minimal diameter of the affected segment. mm	0.82±0.65	0.72±0.59	0.66±0.52	0.001
Percentage of stenosis	75±12%	77±11%	79±12%	0.005

Table 3. The immediate results of revascularization using BMS.

Parameter	Group 1 (n=466)	Group 2 (n=223)	Group 3 (n=38)	P
Number of revascularized stenoses	802	288	51	-
Total amount of target vessels	852	341	86	-
Completeness of revascularization	0.941	0.845	0.837	0.001
Number of treated vessels per patient	1.72	1.29	1.08	0.001
Number of stents per patient	1.84	1.34	1.14	0.001
The amount of administered contrast media, ml	493±84	304±39	237±34	0.001
Increase of vessel diameter, mm	2.36±0.71	2.23±0.54	2.32±0.64	NS
Percentage of stenosis	6.9±5.1%	8.5±4.3%	10.3±9.4%	0.05
Immediate success	99.4%	98.2%	97.4%	NS

Table 4. The immediate results of revascularization using DES.

Parameter	Group 1 (n=271)	Group 2 (n=132)	Group 3 (n=29)	P
Number of revascularized stenoses	421	212	44	-
Total amount of target vessels	457	241	54	-
Completeness of revascularization	0.921	0.880	0.815	NS
Number of treated vessels per patient	1.55	1.60	1.52	NS
Number of stents per patient	1.66	1.67	1.61	NS
The amount of administered contrast media. ml	545±79	301±42	226±39	0.001
Increase of vessel diameter. mm	2.22±0.64	2.14±0.61	2.19±0.57	NS
Percentage of stenosis	5.4±4.8%	6.9±5.3%	6.3±6.0%	NS
Immediate success	99.6%	98.4%	96.6%	NS

STUDY RESULTS

Immediate results. The stenting of the main branch was usually performed in presence of bifurcation lesion. The immediate results of PCI with implantation of BMS are presented in Table 3, and the results of PCI with implantation of DES are presented in Table 4. The smallest residual stenosis was observed in group 1, the largest – in group 3 for both stent types. The biggest differences in immediate results appeared to be the amount of administered contrast media ($p<0.001$), which was limited in group 2 and strictly limited in group 3. Therefore, the number of treated vessels (per patient) for both stent types was less in groups 2 and 3. Naturally, this value was caused by the character of coronary lesion, and in groups 2 and 3 there were lower number of patients with two-vessel or three vessel lesion compared to group 1, because the patients with multi-vessel lesion and severely decreased GFR were more often referred to perform open coronary artery bypass grafting. Nevertheless, the index of completeness of revascularization was relatively higher in group 1, in which we did not have significant limitations of using contrast media, compared to indices in group 2 and 3.

In 2004, 1477 standard stents were implanted during PCI in group 1 (Table 3), 387 BMS were implanted in group 2 and 47 BMS were implanted in group 3. In 2005, 451 drug-eluting stents were implanted in 1271 patients in group 1 (Table 4), 221 stents - in group 2 and 47 stents - in group 3. All implantation were elective. Maximum pressure in balloon during stent dilation was 12 to 20 ATM with mean of 13.6±1.9 ATM. Optimal stent implantation required 2 to 4 dilations with mean of 2.78±0.68 dilations. The need for additional stent implantation occurred rarely.

The majority of standard stents were successfully implanted without dissections D-F, occlusions and “no reflow” phenomenon. The optimal results of PCI with implantation of BMS (residual stenosis less than 20% with blood flow TIMI 3) was not achieved in 3 patients in group 1, in 4 patients in group 2 and in 1 patient in group 3. Thus, the direct success of BMS implantation comprised 99.4%, 98.2% and 97.4% in groups, respectively (differences is not significant). The majority of stents eluting sirolimus or paclitaxel was also successfully implanted. The optimal results of PCI with implantation of DES were not achieved only in 1 patient in group 1, in 2 patients in group 2 and in 1 patient in group 3. Thus, the direct success of DES implantation comprised 99.6%, 98.4% and 96.6% in groups, respectively (differences is not significant). All the patients were alive and transferred to the ward for observation.

Table 5. In-hospital results of revascularization using BMS.

Parameter	Group 1 (n=466)	Group 2 (n=223)	Group 3 (n=38)	P
Discharged patients	465	221	37	-
In-hospital ACS (MI/UA)	2 (0.4%)	6 (2.7%)	2 (5.3%)	0.018
Contrast-induced ARF	2 (0.4%)	11 (4.9%)	5 (13.2%)	0.001
Massive bleeding	2 (0.4%)	3 (1.3%)	1 (2.6%)	NS
Hemotransfusion	2 (0.4%)	3 (1.3%)	1 (2.6%)	NS
Subacute thrombosis	2 (0.4%)	6 (2.7%)	2 (5.3%)	0.018
Repeat revascularizations	2 (0.4%)	6 (2.7%)	2 (5.3%)	0.018
Non-fatal complications	5 (1.1%)	18 (8.1%)	7 (18.4%)	0.001
In-hospital mortality	1 (0.2%)	2 (0.9%)	1 (2.6%)	NS

Table 6. In-hospital results of revascularization using DES.

Parameter	Group 1 (n=271)	Group 2 (n=132)	Group 3 (n=29)	P
Discharged patients	271	131	28	-
In-hospital ACS (MI/UA)	1 (0.4%)	3 (2.3%)	2 (6.8%)	NS
Contrast-induced ARF	2 (0.7%)	9 (6.8%)	5 (17.2%)	0.001
Massive bleeding	1 (0.4%)	2 (1.5%)	1 (3.4%)	NS
Hemotransfusion	1 (0.4%)	2 (1.5%)	1 (3.4%)	NS
Subacute thrombosis	1 (0.4%)	3 (2.3%)	2 (6.8%)	NS
Repeat revascularizations	1 (0.4%)	6 (2.7%)	2 (6.8%)	NS
In-hospital mortality	0	1 (0.8%)	1 (3.4%)	NS
Non-fatal complications	4 (1.5%)	13 (9.8%)	6 (20.7%)	0.001

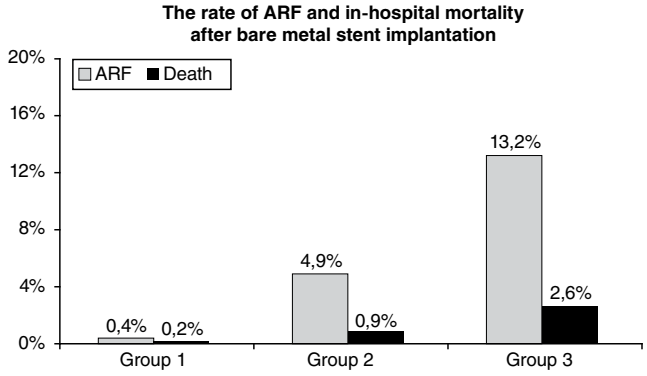

Figure 1. The rate of acute renal failure and in-hospital mortality after PCI using bare metal stents.

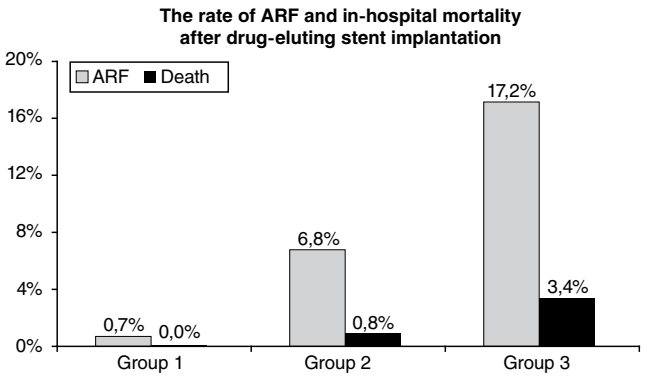

Figure 2. The rate of acute renal failure and in-hospital mortality after PCI using drug-eluting stents.

IN-HOSPITAL OUTCOMES

During 3 days after implantation of BMS, the contrast-induced ARF developed in 2 patients in group 1 (0.4%), in 11 patients in group 2 (4.9%) and in 5 patients in group 3 (13.2%, p<0.001 for trend) despite the prophylaxis (Table 5 and Figure 1). During 3 days after implantation of DES (Table 6 and Figure 2) the contrast-induced ARF developed in 2 patients in group 1 (0.7%), in 9 patients in group 2 (6.8%) and in 5 patients in group 3 (17.2%, p<0.001 for trend)

In case of ARF development the patients initially received mannitol or furosemide in combination with small doses of dopamine for renal blood flow normalization, with following correction of hyperhydration, hyperkalemia and uremia. All the patients with acute renal disorders were consulted by nephrologists and were further cured by cardiologist and nephrologist.

Moreover, during 2 days after implantation of BMS, the subacute thrombosis developed in 2 patients in group 1 (0.4%), in 6 patients in group 2 (2.7%) and in 2 patients in group 3 (5.3%) (p<0.01). This led to acute coronary syndrome (MI with ST elevation or MI without ST elevation/UA) in groups in 2, 6 and 2 cases, respectively. After the PCI with implantation of drug-eluting stent, subacute thrombosis developed in 1 patient in group 1 (0.4%), in 3 patients in group 2 (2.3%) and in 2 patients in group 3 (6.8%) (difference is not significant). This led to acute coronary syndrome (MI with ST elevation or MI without ST elevation/UA) in groups in 1.3 and 2 cases, respectively.

In all cases of ACS development the patients were directed to cath lab repeatedly and the operation on thrombosed vessel was performed against the background of bolus and following infusion of platelet IIb/IIIa glycoprotein receptor blocker (tirofiban). After the implantation of standard stents the repeated PCI was successful in 1 case in group 1 (0.2%), in 4 cases in group 2 (1.8%) and in 1 case in group 3 (2.6%), and unsuccessful and lethal in 1 case in group 1 (0.2%), in 2 cases in group 2 (0.9%) and in 1 case in group 3 (2.6%). After the implantation of drug-eluting stent the repeated PCI was successful in 1 case in group 1 (0.4%), in 2 cases in group 2 (1.5%) and in 1 case in group 3 (3.4%), and unsuccessful and lethal in 1 case in group 2 (0.8%) and in 1 cases in group 3 (3.4%). All in-hospital results of revascularization using BMS are presented in Table 5, and results of revascularization using DES are presented in Table 6.

Thus, after BMS implantation during the next hospitalization the fatal complications occurred (Figure 1) in group 1 with the rate of 0.2%, in group 2 with the rate of 0.9% and in group 3 with the rate of 2.6%, non-fatal complications occurred with the rate of 1.1%, 8.1% and 18.4% in groups, respectively (p<0.001). After the implantation of DES the fatal complications (Figure 2) occurred in group 2 with the rate of 0.8% and in group 3 with the rate of 3.4%, non-fatal complications occurred with the rate of 1.5%, 9.8% and 20.7% in groups, respectively (p<0.001).

DISCUSSION

The majority of patients who underwent administration of contrast media did not develop side effects or complications. However, in case of ARF development, the prognosis worsens significantly. Such patients more often experience various types of in-hospital complications including severe cardiac complications and events, strokes, bleedings/haematomas etc.

Acute renal failure is characterized by rapid decrease of glomerular filtration rate clinically manifested as dramatic and stable increase of urea and creatinine levels. The life-threatening sequelae of ARF are fluid overload, hyperkalemia and metabolic acidosis. ARF is often preventable and, therefore, it is extremely important to reveal the high-risk patients and provide them with appropriate care. One should remember that in case of raising or already developed ARF the fast diagnostic and treatment may prevent the irreversible nephron death (12).

In majority of cases, the treatment of initial stages of ARF is conducted by non specialists. Therefore, all physicians must be able to recognize the symptoms and signs of ARF, prescribe and interpret the investigations and results, begin appropriate treatment and know when and how fast the patient should be referred to more skilled colleagues or specialists (12).

ARF comprises 1% of hospitalizations, and ARF complications comprise more than 7% of total number of in-hospital treatment cases (7, 13), most often in patients with chronic kidney disease. When the patient's state is severe and the dialysis is required, in-hospital mortality comprises 50%, and in septic and critically ill patients it raises up to 75% (14, 15, 16).

It has been previously shown that the risk of death significantly increased in patients who developed contrast-induced acute renal failure (17, 18, 19). In large retrospective study including more than 16000 patients hospitalized and underwent contrast investigations, 183 patients developed contrast-induced acute renal failure (with increase in serum creatinine level more than by 25% from baseline) (20). The mortality rate increased up to 34% after ARF, which was 5.5 times more than mortality rate in patients without ARF, taking into account adjustment for other diseases. High rate of in-hospital mortality related to contrast-induced ARF was observed in other retrospective analysis of 7586 patients, 3.3% of which experienced ARF (2). Among patients experiencing ARF after administration of contrast agent in the body, the in-hospital mortality was 22%, while among other patients (without ARF) mortality rate was 1.4% (2).

It is remarkable to note that in majority of studies the serum creatinine (Cr) and its estimated clearance were used as renal function criteria (usually by Cockroft-Gault method). Thus, in the study in which serum creatinine was used as a criterion (baseline Cr 1.8 mg/dl), the contrast-induced ARF (defined as increase of Cr by more than by 25% from baseline) observed after PCI in 37% of 439 patients (21). After ARF development the in-hospital mortality comprised 14.9% compared to 4.9% in patients without ARF ($p<0.001$). However, these parameters are not the precise markers of renal function and its disorders. The glomerular filtration rate is the most appropriate parameter for renal function estimation (10).

Unfortunately, in the global literature resources we did not find the studies evaluating in-hospital outcomes in patients underwent PCI with DES implantation having moderate or severe renal function impairment, but in those who did not undergo hemodialysis before PCI. A few studies reflected only the results of PCI with DES implantation in patients on dialysis. Naturally, this critically severe category of patients should be carefully studied as the rate of ARF and deaths after PCI in patients on dialysis is extremely high. Thus, the mortality increased up to 35.7% in patients who underwent dialysis before PCI compared to 7.1% in patients who underwent PCI and ARF who did not have dialysis previously (18). Fortunately, the number of patients who have been stented and received dialysis is small. There is much greater number of patients undergoing PCI due to CHD with moderately impaired renal function, who did not require hemodialysis before coronary intervention. The structure of in-hospital complications in this patients` category is not within the scope of investigators interest, whereas the drug-eluting stents are massively implanted.

The role of kidney function was not evaluated until recently in patients who underwent PCI with implantation of DES. Only in 2009 the EVENT (Evaluation of Drug Eluting Stents and Ischemic Events) registry analysis have been presented (22). Depending on baseline creatinine clearance (CC), 4791 patients who underwent BMS implantation were stratified into 4 groups: >75 (n=2827), from 50 to 75 (n=1253), from 30 to 49 (n=571) and <30 ml/min (n=140). The DES were implanted in 84.3% - 89.5% of patients in different groups, BMS + DES were implanted in 3.5% - 5.0% of patients and BMS only were implanted in 6.1% - 8.6% of patients. The in-hospital mortality in groups of patients with CC >75, from 50 to 75, from 30 to 49 and <30 ml/min comprised 0.1%, 0.2%, 0.9% and 0.0%, respectively. Non-fatal in-hospital MI occurred in groups in 5.7%, 7.3%, 8.2% and 10.0% of cases, respectively. However, the rate of ARF was not presented in the study.

In this study we have shown that along with decrease of baseline renal function impairment, estimated using GFR, the ARF rate is increasing despite the prevention of contrast-induced complications. This growth of ARF incidence does not depend on the type of implanted stent (BMS or DES) and occurs when using bare metal stents and drug-eluting stents as well. However, there was not significant mortality growth detected, and increase of percentage of mortality is associated with decrease of number of patients in groups parallel to decrease of GFR. If speculate, it can be supposed that the absence of increased mortality is partially due to preventive measures (hydration, acetylcysteine) performed

before PCI, and due to limitation of administered contrast agent quantity during interventions.

Moreover, it is interesting that in groups of patients who underwent implantation of standard stents, the growth of other non-fatal complications (except ARF) rate was observed parallel to decrease of GFR while in groups of patients who underwent implantation of drug-eluting stents only the growth of ARF rate was observed. It is possible that revealed differences in the rate of in-hospital events depending on stent types are due to big number of patients in groups, who underwent implantation of standard stents, and this number led to significant differences concerning other complications.

Eventually, the prevention of ARF in groups of patients with moderate or severe decreased baseline GFR should be recognized as insufficient. Unfortunately, the evidence-based reasoning for other prevention strategies is small or the data from various studies are controversial. It is very important that parallel to growth of ARF rate there was no significant increase of in-hospital mortality. Nevertheless, the contrast-induced complications remains the most significant factors limiting the clinical success of percutaneous interventions with implantation of any types of stents.

CONCLUSIONS

1. The decreased baseline glomerular filtration rate as a renal function parameter leads to increased rate of acute renal failure after percutaneous coronary interventions.
2. The significant growth of ARF incidence occurs after implantation of any type of stents.
3. In setting of initial ARF prevention and limitation of administered contrast agent quantity for patients with decreased GFR before PCI, there is no significant increase of in-hospital mortality.

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Cardiorenal Syndromes in Invasive Cardiology. Long-Term Outcomes of Elective Coronary Interventions in Patients with Coronary Atherosclerosis and Chronic Kidney Disease

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SUMMARY

This study included 432 patients who underwent elective percutaneous coronary interventions (PCI) with drug-eluting stents (DES) implantation. The patients were divided into three groups according to initial glomerular filtration rate (GFR): the 1st group with GFR ⩾ 60 ml/min/1.73 m^2, the 2nd group with GFR from 30 to 60 ml/min/1.73 m^2, and the 3rd group with GFR < 30 ml/min/1.73 m^2. Thus, the 2nd and 3rd groups belonged to the 4th type of cardiorenal syndrome (CRS). The contrast media iodixanol was used during angiography. Prevention of the 3rd type of CRS –contrast induced nephropathy (CIN) was performed in all patients. Immediately success of PCI was high in all groups. CIN incidence after PCI was significantly higher in the 2nd and the 3rd groups. Within 12 months of follow up the rate of target vessel restenosis and repeat revascularizations was higher in the 2nd and the 3rd groups: 15.9 and 27.9% vs 6.6% in the 1st group (p<0.001). Decreased GFR was the predictor of late death within 3 years: relative risk (RR) for group 2 was 1.77 (95%CI 1.19 ÷3.74; p=0.001), RR for group 3 was 3.69 (95% CI 1.58÷6.87; p=0.001). Besides that reduced GFR was the predictor of non-fatal MI up to 3 years: relative risk (RR) for group 2 was 1.69 (95% CI 1.12 ÷3.07; p=0.009) and RR for group 3 was 3.44 (95% CI 1.37÷6.19; p=0.001). Thus, the presence of the 4th CRS type in patients (with initially reduced GFR) after PCI increases the risk of CIN, leads to increase the rate of restenosis and repeat revascularizations within 12 months and is considers to be a predictor of late death within up to 3 years and non-fatal MI.

Keywords: cardiorenal syndrome (CRS), chronic kidney disease (CKD), glomerular filtration rate (GFR), percutaneous coronary interventions (PCI), contrast-induced nephropathy (CIN).

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INTRODUCTION

Until recently the term "cardiorenal syndrome" (CRS) was used widely without adequate definition. To include a big multiplicity of interrelated disorders and to underline two-directional character of cardiorenal interactions the new classification of CRS with 5 subtypes was lately proposed, in which pathological physiology, lesion duration, and character of concomitant cardiac and renal dysfunctions were reflected (1).

CRS can generally be determined as pathological physiological disorder of heart and kidneys, and therefore an acute or chronic dysfunction of one organ can cause an acute or chronic dysfunction of another organ (2). The 1st type of CRS (acute cardiorenal syndrome) reflects a dramatic cardiac function deterioration (for example, acute cardiac failure including acute coronary syndrome or decompensation of congestive chronic heart failure) leading to acute damage of kidneys. The 2nd type of CRS (chronic cardiorenal syndrome) includes chronic disturbances of cardiac function (e.g. chronic congestive heart failure) causing progressive development of chronic kidney disease (CKD). The 3rd type of CRS (acute renocardial syndrome) develops due to strong deterioration of kidney function (e.g. acute renal ischemia or glomerulonephritis) causing an acute cardiac dysfunction (e.g. acute heart failure, arrhythmias, ischemia). The 4th type of CRS (chronic renocardial syndrome) describes the condition of chronic kidney diseases (e.g. chronic glomerulonephritis) causing a reduction of cardiac function, left ventricular hypertrophy and/or increased risk of adverse cardiovascular events. The 5th type of CRS (secondary cardiorenal syndromes) reflects the systemic condition (e.g. sepsis) causing cardiac and renal dysfunction (3).

Biomarkers can help early diagnosis of CRS and allow to prescribe the treatment timely. Use of this classification characterizes groups of patients quite completely, provides the choice of treatment strategies, allows to stratify patients referred to different examination (1, 2).

In interventional cardiology, in patients with acute cardiac decompensation (acute coronary syndrome: myocardial infarction or unstable angina) the con-

trast-induced acute renal failure (ARF) after diagnostic angiography or percutaneous coronary intervention refer to 1st type of CRS. The 3rd type of CRS includes a development of contrast-induced ARF after planned coronary angiography or elective (planned) percutaneous coronary intervention (PCI) in patients without previous renal abnormalities. Contrast vascular procedures in patients with chronic kidney disease causing acute renal failure with further cardiac decompensation and leading to long-term adverse events and complications are included in the 4th type of CRS.

During some past decades many clinical trial focused to the search of methods and drugs of contrast-induced nephropathy prevention were performed (4-8). Majority of data from retrospective studies indicates to severe relation of contrast induced nephropathy (CIN) with unfavourable immediate outcomes including death. Long-term outcomes after CIN were studied less (9). At the same time, the increased risk of ARF development in patients with CKD should not became the reason of contrast heart examination refusal. Thus, for 4th type of CRS (in patients with CKD) it is reasonable to minimize the risk of CIN development. Particularly drug-eluting stent use in CKD patients allows to reduce the incidence of repeated PCI and thus, the necessity of repeated contrast media administration (10). This study is dedicated to assessment of long-term outcomes of PCI with DES implantation in patients with CKD.

MATHERIALS AND METHODS

In this study we included 432 patients, who underwent planned PCI with one or more DES implantation in 2005. The study enrolled patients with stable angina (II- IV class according to CCS classification) or with acute coronary syndrome (unstable angina with negative biochemical cardiac markers), which was stabilized prior to angiography. A part of patients had 4th type of CRS - CHD coupled with CKD (with decrease of renal function or without glomerular filtration rate reduction).

All patients included in the study had no previous hemodyalisis procedures. Another reason of patient's discontinuation was history of any revascularization procedures (stenting or bypass surgery). Patients with main left coronary artery lesion, patients within the 7 first days of MI with ST-segment elevation or MI without ST elevation but with positive cardiac markers ("troponin-positive" MI) were excluded from the study as well. Patients with aspirin and clopidogrel intolerance, allergy to contrast agent were also excluded from the study. Angiographic exclusion criterion was vessel reference diameter at the site of stenosis less than 2.5 mm or more than 4.5 mm, vessel kink at the site of stenosis greater than 60°. Patients gave written informed consent to intervention prior to treatment.

To characterize renal functional condition criteria of K/DOQI Guidelines (2002) were used (11). According to these Guidelines *CKD consists of*: a) kidney damage within ⩾ 3 months with GFR decrease or b) GFR < 60 ml/min/1.73 m^2 within ⩾ 3 months with renal damage or without it.

Contrast-induced nephropathy (CIN) according to the commonly accepted criteria was identified in case of relative increase of more than 25% or in case of absolute increase of serum creatinine by more than 0.5 mg/dl from baseline value within 48 72 hours after contrast administration (11).

In order to assess the long-term results patients were followed-up for up to 36 months post stenting. Patients who underwent PCI without any in-hospital complications were invited to return for clinical follow-up. In case of recurrent angina or other complications patients were hospitalized for assessment of changes and considering possibility of repeated interventions. At the end of follow-up (36 months) all patients who did not returned after index hospitalization were questioned by telephone.

STATISTICAL ANALYSIS

Study results were processed using BioStat (S.Glanz ©, USA 1999), Statistica for Windows 6.0 (StatSoft Inc., USA 2001). In case of normal distribution univariate analysis of variance (ANOVA) was used for primary data comparison between groups. If normality of distribution did not confirm the ordinal Mann-Whitney or Kruskall-Wallis criteria were used. Chi-square test or exact Fisher's test were used for quality signs assessment. Proportions were compared using z-test with Yates correction or Fisher's exact test. Relations between parameters were revealed by Pearson or Spearman correlation analysis and by different regression models with determination of significant relative risk predictors (95% CI) as well. Assessment of representativeness of obtained results were performed for all types of analysis. P-values of <0.05 were considered as statistically significant

CLINICAL AND ANGIOGRAPHIC CHARACTERISTICS OF PATIENTS

Patients included into the study were divided into 3 groups according to glomerular filtration rate estimated prior to PCI (Table1). 1). GFR calculations were performed using MDRD formula: group with normal GFR (undamaged kidneys and 4th type of CRS – CKD stage 1-2) consisted of patients with GFR > 60 ml/min/1.73m^2, group with moderate GFR reduction (4th type of CRS – CKD stage 3) consisted of patients with GFR from 30 to 60 ml/min/1.73 m^2, group with severe renal dysfunction (4th type of CRS - CKD stage 4) consisted of patients with GFR < 30 ml/min/1.73 m^2 (table 1). Group 1 that included 271 patients with GFR > 60 ml/min/1.73 m^2 contained of 51 patients with CKD stage 1 and 2 (without GFR decrease), i.e. that patients had 4th type of CRS – kidney damage during > 3 months manifesting with one of known signs.

Main clinical data of patients are shown in Table 1.

Patients age ranged from 34 to 80 years with mean of 58±12 years. ARF prevention was performed in all patients prior to coronary angiography and PCI. To do this, an adequate patients' hydration (100 ml/hrs of liquid) 4 hours prior to and within 24 hours after angiography and prevention of nephrotoxic medication intake were performed. In addition, N-acetylcysteine at a dose of 600 mg/day was prescribed 48 hours prior to invasive examination. Non-ion isoosmolar contrast media iodixanol was used only; we considered it necessary to limit and to reduce its amount where possible. The total amount of contrast for diagnostic coronary angiography and stenting did not exceed 350 ml if GFR was from 45 to 59 ml/min/1.73 m^2 and 250 ml if GFR was less than 45 ml/min/1.73 m^2. Sum amount of contrast for coronary angiography and PCI did not exceed 600 ml in all patients with GFR > 60 ml/min/1.73 m^2. For ARF preventions in all patients with decreased GFR (< 60 ml/min/1.73 m^2 – groups 2 and 3) coronary stenting was performed within 3-5 days after coronary angiography based on creatinine changes monitoring, and in 220 patients from group 1 with normal and or slightly decreased GFR (> 60 ml/min/1.73 m^2) PCI was performed simultaneously with coronary angiography.

Main baseline angiographic values are shown in Table 2.

RESULTS

Immediate results. Immediate PCI results are presented in Table 3. Immediate results differences were manifested in contrast media administered amount ($p<0.001$) which was limited in group 2 and strictly limited in group 3. Completeness of revascularization index was slightly higher in group 1 (0.921) where we had no significant limitations of contrast agent amount compared to indices in group 2 (0.880) and group 3 (0.815).

During interventions sirolimus-eluting stents or paclitaxel-eluting stents were used. Intervention parameters are shown in Table 3. Need for implantation of additional stent appeared rarely. Immediate success of stent implantation was 99.6%, 98.4% and 96.6%, respectively in groups (differences are not significant), and all patients were alive and transferred under observation to a ward.

In-hospital outcomes. All hospital events are shown in Table 4. Despite performed prevention within 2 3 days after PCI the contrast-induced nephropathy was developed in 2 patients in group 1 (0.7%), in 9 patients in group 2 (6.8%) and in 5 patients in group 3 (17.2%) ($p<0.001$). If CIN occurs patients were treated by mannitol or furosemide combined with low doses of dopamine to restore normal renal blood flow and then hyperhydration, hyperkalemia and uremia were corrected.

Thus, during further hospitalization fatal complications were happened in 0.8% of patients in group

Table 1. Baseline clinical data.

Parameter	Group 1 (n=271)	Group 2 (n=132)	Group 3 (n=29)	P
Renal function characteristics	GFR of ⩾ 60 ml/min/1.73m^2	GFR from 30 to 60 ml/min/1.73m^2	GFR of < 30 ml/min/1.73m^2	
Males	211 (78%)	101 (77%)	20 (69%)	NS
Smokers	102 (38%)	57 (43%)	12 (41%)	NS
Diabetes mellitus	47 (17%)*	38 (29%)*	9 (31%)	*0.008
Arterial hypertension	169 (62%)	103 (78%)	27 (93%)	0.002
Hypercholesterolemia	137 (51%)	79 (60%)	19 (66%)	NS
Prior MI	49 (18%)	45 (34%)	11 (37%)	0.028
CF	35 (13%)	21 (16%)	6 (21%)	NS

Table 2. Baseline angiographic data.

Parameter	Group 1 (n=271)	Group 2 (n=132)	Group 3 (n=29)	P
Single-vessel disease	144 (53%)*	49 (37%)*	12 (41%)	*0.004
Two-vessel disease	68 (25%)*	57 (43%)*	9 (31%)	*0.001
Three-vessel disease	59 (22%)	26 (20%)	8 (28%)	NS
Total amount of target vessels	457	241	54	-
Stenosis length. mm	17±5	18±6	16±8	NS
Reference diameter of the target segment. mm	3.12±0.53*	2.99±0.59*	2.94±0.61	*0.027
Minimal diameter of the target segment. mm	0.79±0.51	0.70±0.55	0.62±0.54	NS
Percentage of stenosis	75±12%	77±11%	79±12%	NS

Table 3. Immediate results of coronary interventions.

Parameter	Group 1 (n=271)	Group 2 (n=132)	Group 3 (n=29)	P
Number of revascularized stenoses	421	212	44	-
Total amount of target vessels	457	241	54	-
Index of Completeness of revascularization	0.921	0.880	0.815	NS
Number of treated vessels per patient	1.55	1.60	1.52	NS
Number of stents per patient	1.66	1.67	1.61	NS
The amount of administered contrast media. ml	545±79	301±42	226±39	0.001
Increase of vessel diameter. mm	2.22±0.64	2.14±0.61	2.19±0.57	NS
Percentage of stenosis	5.4±4.8%	6.9±5.3%	6.3±6.0%	NS
Immediate success	99.4%	98.2%	97.4%	NS

Table 4. Hospital results of coronary interventions.

Parameter	Group 1 (n=271)	Group 2 (n=132)	Group 3 (n=29)	P
Discharged patients	271	131	28	-
In-hospital ACS (MI/UA)	1 (0.4%)	3 (2.3%)	2 (6.8%)	NS
Contrast-induced ARF	2 (0.7%)	9 (6.8%)	5 (17.2%)	0.001
Massive bleedings	1 (0.4%)	2 (1.5%)	1 (3.4%)	NS
Hemotransfusion	1 (0.4%)	2 (1.5%)	1 (3.4%)	NS
Subacute thrombosis	1 (0.4%)	3 (2.3%)	2 (6.8%)	NS
Repeat revascularizations	1 (0.4%)	6 (2.7%)	2 (6.8%)	NS
In-hospital mortality	0	1 (0.8%)	1 (3.4%)	NS
Non-fatal complications	4 (1.5%)	13 (9.8%)	6 (20.7%)	0.001

Table 5. Long-term up to 3 years results of coronary interventions.

Parameter	Group 1 (n=271)	Group 2 (n=131)	Group 3 (n=28)	P
Survived to 3 years	260 (95.9%)	122 (92.4%)	25 (86.2%)	0.05
Died to 3 years	11 (4.1%)	10 (7.6%)	4 (13.8%)	0.05
Non-fatal complications	33 (12.2%)	33 (25%)	13 (44.8%)	0.001
Restenosis to 12 months	18 (6.6%)	21 (15.9%)	8 (27.6%)	0.001
Repeat PCI to 12 months	16 (5.9%)	18 (13.6%)	6 (20.7%)	0.003
Bypass surgery within 12 months	2 (0.7%)	3 (2.3%)	2 (6.9%)	0.03
Rethrombosis of target vessel to 3 years	3 (1.1%)	5 (3.8%)	2 (6.9%)	NS
MI/UA to 3 years	15 (5.5%)	12 (9.1%)	5 (17.2%)	0.041

Table 6. MI and death incidence within 3 years with respect of CIN.

Group	Risk of MI compared with group 1	Death risk compared with group 1
1	1	1
2	1.69	1.77
3	3.44	3.69

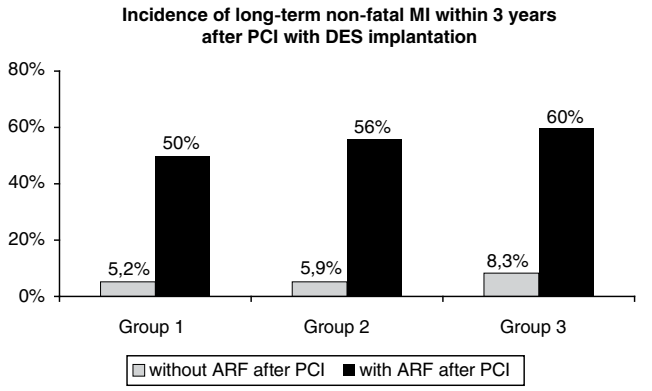

Figure 1. Incidence of non-fatal MI within 3 years after drug-eluting stent implantation with respect to in-hospital ARF development.

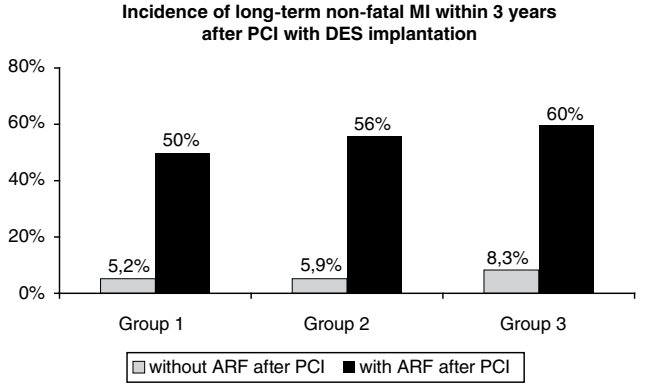

Figure 2. Incidence of long-term mortality within 3 years after drug-eluting stent implantation with respect of in-hospital ARF development.

2 and in 3.4% of patients in group 3 and non-fatal complications were occurred in 1.5%, 9.8%, 20.7% in groups 1, 2, 3 respectively ($p<0.001$).

Long-term results. After discharge, during follow-up of up to 12 months 18 patients from group 1 (6.6%), 21 patients in group 2 (15.9%) and 8 patients in group 3 (27.6%) returned due to recurrent angina (table 5). Hemodynamically significant restenosis was revealed in them during the control coronary angiography. All patients with restenosis were revascularized repeatedly. They underwent PCI in target lesions or, in case of two or three-vessel disease, had got coronary artery bypass grafting.

During observation to 3 years the target vessel rethrombosis occurred in 3 cases (1.1%) in group 1, in 5 cases (3.8%) in group 2, and in 2 cases (6.9%) in group 2. It was the one of ACS development reasons (MI or UA) which observed in 15 patients of group 1 (5.5%), in 12 patients of group 2 (9.1%) and in 5 patients of group 3 (17.2%). Within 3 years of observation 11 patients (4.1%) have died in group 1 from cardiac and non-cardiac reasons, 10 patients (7.6%) – in group 2, 4 patients (13.8%) – in group 3. Table 5 shows all long-term results.

Review of events within 3 years with respect of contast-induced nephropathy during the first hospitalization revealed that CIN occurred in 2 cases in group 1, in 9 cases in group 2 and in 5 cases in group 3. Analysis demonstrated that MI incidence within 3 years raised 1.69 times more in group 2 vs group 1 and 3.44 times more in group 3 vs group 1.

When dividing the patients into groups depending on CIN development the very high incidence of post CIN myocardial infarction (50% to 60%) was observed in all three groups and a slight increase of MI incidence from group 1 to group 3 (from 5.2% to 8.3%) was revealed if CIN did not develop (Table 6 and Figure.1). Mortality analysis showed that death incidence within 3 years was generally increased 1.77 times in group 2 vs group 1 and 3.69 times in group 3 vs group 1. Patients distribution into groups according to CIN development revealed the same high post CIN death rate in all three groups (from 50% to 60%) and minimal increase of death incidence from group 1 to group 3 (from 3.7% to 4.2%) if CIN did not develop (Table 6 and Figure 2).

In groups of patients with 4th type of CRS (CKD) initially decreased GFR was a predictor of late death within 3 years. Relative death risk was 1.77 (95%CI 1.19÷3.74, p=0.001) for group 2 vs group 1, RR of death was 3.69 (95% CI 1.58÷6.87, p=0.001) for group 3 vs group 1. Simultaneously in groups of patients with 4th type of CRS (CKD) initial decreased GFR was a predictor of non-fatal MI within 3 years. Relative risk of myocardial infarction was 1.69 (95%CI 1.12÷3.07, p=0.009) for group 2 vs group 1, RR of MI was 3.44 (95% CI 1.37÷6.19, p=0.001) for group 3 vs group 1.

DISCUSSION

The recent randomized studies demonstrated that the use of drug-eluting stents decreases significantly the incidence of stent restenosis (13, 14). However, cardiorenal syndrome is usually an exclusion criterion for prospective randomized studies, as chronic kidney disease including terminal renal failure influences substantially on CHD course and worsens the prognosis for these patients. In many studies it

was shown that 4th type of CRS (moderate or severe CKD, concurrent CHD) is widely spread, and patients with CHD undergoing revascularization belong to the group of high risk (15, 16, 17, 18). It should be noted that CKD is associated with high incidence of adverse cardiac complications and events, acute renal failure and restenosis after PCI (16, 18, 19).

Thus, our study revealed that ARF within first 2-3 days after stenting developed more often in case of baseline cardiorenal syndrome – 17.2% in patients with GFR < 30 ml/min/1.73 m^2 (group 3) vs 6.8% in patients with GFR from 30 to 60 ml/min/1.73 m^2 (group 2) and 0.7% in group 1 (GFR > 60 ml/min/1.73 m^2), p<0.001. The similar trend was revealed for the subacute thrombosis developing within up to 48 hours after PCI. Thus, in groups 2 and 3 subacute thrombosis occurred insignificantly often vs group 1 (6.8% and 2.3% vs 0.4%). Subacute thrombosis caused ACS (MI with ST elevation or MI without ST elevation / UA) respectively in 1, 3 and 2 patients. But only in 1 case in group 2 (0.8%) and in 1 case in group 3 (3.4%) thrombosis treatment had fatal outcome. In other patients repeated PCIs were completed successfully.

When assessing the restenosis rate within 12 months the following data were obtained: in group 3 restenosis rate was 27.6% vs 15.9% and 6.6% in groups 2 and 1, respectively (p<0.001).

The similar data were received in the study performed by Ota T. et al, (20) where the influence of different stage of renal failure on angiographic and clinical outcomes of DES implantation was evaluated. In hemodialysis patients the restenosis rate was 40% vs 11.5% in patients with GFR < 60 ml/min/1.73 m^2 and 10.4% in GFR ⩾60 ml/min/1.73 m^2. In this study, the rate of target vessels revascularization was higher in hemodialysis patients as well – 23.5% compared to two other groups (9.2% and 8.1% respectively (p=0.016)).

In the study of Ota T. Et al. (20) a mortality rate as in our study was higher in patients with CRS (marked CKD): 11.8% vs 2.3% and 0.6% respectively in groups of hemodialysis, GFR < 60 ml/min/1.73 m^2 and GFR ⩾60 ml/min/1.73 m^2 (p<0.001).

Results obtained in the study of Zhang R.Y. et al. were comparable with our data (9). Patients were divided according to CRS presence: (group of CKD with GFR < 60 ml/min/1.73 m^2 (n=410) and control group with GFR > 60 ml/min/1.73 m^2 (n=602)) and according to stents implanted: DES (n=264) or bare metal stent (n=146). During observation (on average 17 months) cardiac mortality rate was significantly higher in patients with CKD (3.4% vs 1.0%, p<0.01). In patients with moderate CKD a DES implantation compared to BMS significantly decreased mortality rate from any reasons (5.3% vs 10.9%, p<0.05) and major adverse cardiac events (15.1% vs 24.6%, p<0.05). Due to that fact the authors made a conclusion that CKD is important clinical factor influencing on post PCI mortality, and DES use in patients with CKD is more preferable because of long-term outcomes improvement in such patients.

In our study, the distribution of patients according to GFR decrease in three groups and patients subgroup separation according to ARF development after PCI allowed to reveal the differences between in-hospital and 3-year long-term outcomes of coronary stenting, demonstrating the potential of drug-eluting stent use in patients with 4th type of cardiorenal syndrome (CHD and CKD) compared to patients with CHD without CRS.

In our opinion, the use of drug-eluting stents ensures significant benefit in patients with cardiorenal syndrome and decreased GFR since they allow to reduce markedly the stent restenosis rate and diminish the rate of repeated interventions. At the same time, as our study has shown planning of percutaneous coronary intervention in patients with 4th type of cardiorenal syndrome (CHD and CKD) in GFR < 30 ml/min/1.73 m^2 or GFR from 30 to 60 ml/min/1.73 m^2 should be mandatory associated with preventive measures directed to reducing of ARF risk. Moreover, the strategy of percutaneous intervention should be planned very carefully in patients with high ARF risk that allows to avoid any unnecessary stages and reduce an amount of contrast agent administered.

CONCLUSIONS

1. Patients with cardiorenal syndrome and decreased glomerular filtration rate are at high risk of acute renal failure development after coronary stenting.
2. Initially decreased glomerular filtration rate is associated with increase of restenosis and repeated revascularizations rate within 12 months after drug-eluting stent implantation.
3. Development of acute renal failure after percutaneous coronary interventions causes further significant increase of non-fatal MI rate and death within 3 years.

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Contrast-Induced Nephropathy. Focus on Prophylaxis.

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SUMMARY

Contrast-induced nephropathy (CIN) is an iatrogenic pathology occurring after the administration of contrast medium in the body. The direct toxic effects on renal tissue and decreased renal hemodynamic are known as pathways of CIN pathogenesis. The other CIN pathogenesis mechanisms are still not well understood. Presently, there are many definitions of CIN, and the most common are the increase in serum creatinine level more than by 0.5 mg/dl or more than by 25% from baseline as measured at 48 or 72 hours after administration of contrast media. CIN occurs rather rarely in general patient` population who underwent contrast enhanced examinations, but occurs much more often in groups of patients with existing renal pathology, diabetes mellitus and in elderly patients. The probability of CIN development is significantly larger in presence of several risk factors. The best methods of CIN prophylaxis are the active detection of patients with risk factors and adequate periprocedural hydration. The role of various drugs in prophylaxis of contrast-induced nephropathy is still disputable and requires further investigation. The iso-osmolar and low-osmolar contrast media are to be used in modern clinical practice for CIN prophylaxis, and high-osmolar contrast media should be strictly avoided in patients with impaired renal function despite the different interpretation concerning the nephrotoxicity of various contrast agents.

Keywords: contrast media, serum creatinine (Cr), creatinine clearance (CC), glomerular filtration rate (GFR), contrast-induced nephropathy (CIN).

INTRODUCTION

The growing use of contrast media in diagnostic and therapeutic radiological procedures led to increased number of cases of contrast-induced nephropathy (CIN) – an iatrogenic pathology related to administration of contrast medium in the body.

CIN is a complex syndrome of acute renal failure occurring after administration of iodine-containing contrast media. CIN is defined as absolute or relative increase in serum creatinine level from baseline after administration of contrast agent if other reasons of impaired renal function are excluded. The increase in creatinine level is observed within 24-48 hours after administration of contrast agent; the peak level of creatinine is observed at 3-5 days after the procedure with returning of creatinine level to normal or close to normal value within 1-3 weeks (1). The magnitude of creatinine level increase as defined for CIN is variable in different studies (20-50% or 0.5-1.0 mg/dl in absolute figures) which makes difficult to compare the results. The definition most commonly used recently include relative increase in serum creatinine level by more than 25% from baseline or absolute increase by more than 0.5 mg/dl from baseline within 48-72 hours after administration of contrast agent in the body. Based on this definition, the incidence of CIN in general population is ranged from 1.2 to 1.6% doe to different reports (2, 3). The incidence of CIN is even higher in patients with different cardiovascular pathology, which is not surprising taking into account the high number of risk factors for CIN development in this group of patients. According to the data of Mayo Clinic, the incidence of CIN in 7586 patients who underwent percutaneous coronary interventions (PCI) was 3.3% (4). In relatively small study conducted by McCullough et al. (5), in which 1826 patients who underwent PCI have been analyzed, CIN was observed in 14.5% of cases. The hemodialysis was required in 0.7% and 0.3% of cases, respectively.

THE PATHOGENESIS OF CONTRAST-INDUSED NEPHROPATHY

The pathogenesis of CIN is not entirely clear. Up to now, there were several pathophysiological mechanisms of CIN proposed including direct toxic impact on renal tubular epithelium, oxidant stress, ischemic impairment and tubular obstruction (6, 7). Russian (8) and foreign nephrologists (9) state that X-ray contrast agents either cause spasm of afferent arteriole aided by renin-angiotensin system after the short period of vasodilatation, and impair microcirculation by increasing the blood viscosity, as well as cause direct toxic effects on tubular epithelium, probably by generation of free oxygen radicals (8, 9). The low blood flow in medullar renal layer leading

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to its hypoxia may be the result of increased peripheral hydrostatic pressure and secondarily increased pressure in tubules due to contrast-induced diuresis, vasoconstriction due to excess of such vasoactive agents as adenosin and endothelin, and decrease of vasodilator levels - nitric oxide and prostaglandins (10, 11). The excretion of contrast medium requires the significant amount of urine in order to lessen the osmotic load. The kidney functioning under conditions of high osmotic load leads to typical histopathological changes called "osmotic nephrosis". The changes typical for osmotic nephrosis were revealed in 22.3% of biopsies performed in patients within 10 days after the administration of contrast media (12). After administration of contrast medium the transient increase in renal blood flow is observed with subsequent continuous decrease in animals and humans (13). Endothelin-1 is considered to be the most likely cause of changes in majority of performed studies (14, 15). The vasoactive effect of adenosin on different organs depends on balance of its receptors – A1 and A2. In kidneys, adenosine causes vasoconstiriction in contrast to the heart. It is also considered to play the role in pathogenesis of CIN due to increased concentration in kidney as a result of intensified hydrolysis of adenosine triphosphate (16). Free oxygen radicals forming under hypoxic conditions are also likely to contribute to renal impairment (17).

RISK FACTORS FOR CONTRAST-INDUCED NEPHROPATHY

CIN risk factors were well studied in several studies and summarized in summary table (Table 1). They can be divided into two categories: fixed (unmodifiable) and modifiable.

Table 1. Risk factors for development of contrast-induced nephropathy.

Fixed (unmodifiable) risk factors	Modifiable risk factors
Age	Decrease of circulating blood volume
Diabetes mellitus	The volume of administered contrast agent
Previous renal failure	Use of nephrotoxic agents (NSAIDs, cyclosporine, aminoglycosides)
Congestive heart failure	Low serum albumin level (<35 g/l)
Unstable hemodynamics	Anemia
Nephrotic syndrome	
Previous renal transplantation	

NSAIDs – non-steroidal anti-inflammatory drugs

The following unmodifiable CIN risk factors are best studied: elderly age, diabetes mellitus, previous renal failure, congestive heart failure, unstable hemodinamics and nephritic syndrome.

Age

The use of contrast enhanced examinations in elderly patients possesses the increased risk for contrast-induced nephropathy. In the study performed by Rich et al. in patients older than 70 years, the CIN developed in 11% of examinations (3). The causes of high risk for CIN development in elderly age were not specially studied and are likely to be multifactorial, including age-related changes in renal function with decreased glomerular filtration rate (GFR), tubular secretion and concentration ability, and also more complicated vessel puncture that requires larger amount of contrast agent, presence of multivessel lesion etc. It is important that age >70 years was the independent predictor for CIN development in multivariate analysis (18, 19, 20).

Previous kidney failure

Chronic kidney failure (CKF) is now included in supranosological conception and is defined as chronic kidney disease (CKD) with increase in serum creatinine level (critical risk factor for CIN development) and extremely high incidence ranging from 14.8% to 55% (4, 5, 21). The multvariate analysis showed that baseline creatinine level was the independent predictor for CIN development in most investigations (3, 4, 5, 21). In contrast, the risk for CIN development was minimal (<10%) in patients with normal renal function during the examination with administration of contrast media.

The high baseline creatinine levels were associated with increased risk of CIN (22). The study performed by Hall et al. (23) showed that the incidence of CIN was only 2% with baseline creatinine levels of <1.2 mg/dl. However, in patients with baseline creatinine level of 1.4-1.9 mg/dl the incidence of CIN increased to 10.4%, and in patients with baseline creatinine level of >2.0 mg/dl CIN developed in 62% cases of angiography. The CIN risk prognosis model by baseline serum creatinine shows exponential increase in nephrotoxicity rate with baseline level of >1.2 mg/dl (24). In general, the estimated value of glomerular filtration rate (GFR) of <60 ml/min/1.73 m2 is considered to be marginal in relation to growing risk of CIN (25).

Diabetes mellitus

In multiple studies (3, 4, 5, 26) the diabetes mellitus (DM) was defined as independent predictor of CIN development. The incidence of CIN in patients with DM is ranged from 5.7 to 29.4% (2, 27, 28). Given the high prevalence of diabetes in general population and its ability to cause the wide spectrum of cardiovascular pathology requiring imaging examinations for correct diagnostic and treatment, patients suffering from DM present a significant portion among subjects undergoing contrast enhanced examinations. It is interesting to note that risk of CIN increases in patients with DM even with preserved renal function (26, 29). The probability of CIN development in patients with DM is further increasing in presence of other risk factors such as renal failure and proteinuria. In the study performed by Berns et al. (1) CIN occurred in 27% of patients with DM with baseline creatinine level of 2.0 4.0 mg/dl and in 81% of patients with DM with baseline creatinine level <4.0 mg/dl. In the study performed by Toprak et al.

(30) the estimated creatinine clearance decreased in 421 patients and ranged from 15 to 60 ml/min according to Cockroft-Gault formula. When dividing the patients into 3 groups depending on fasting blood glucose level, CIN (defined as increase in creatinine level by more than 25% from baseline within 48 hours after angiography) occurred in 5.5% of patients in group with normal fasting blood glucose levels (n = 144; glucose level < 100 mg/dl), in 11.4% of patients with prediabetic state (n = 140; glucose level 100-125 mg/dl) and in 20% of patients with DM (n = 137; glucose level > 125 mg/dl) (30).

Congestive heart failure and unstable hemodinamics

As the reduced renal perfusion is considered to be the most likely mechanism of renal impairment in CIN, it is not surprising that certain clinical conditions leading to worsening of hemodinamics predispose to CIN development. Congestive heart failure was associated with increased risk of CIN in several studies (3, 4, 26, 31). Anterior myocardial infarction (well known factor of worsening of hemodynamics), as well as hypotension during angiography and use of intra-aortic balloon pump (IABP) counterpulsation were the independent causes of CIN in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention (31, 32).

Anemia

In the large registry including 6773 patients which subsequently who underwent percutaneous coronary intervention, the low baseline hematocrit was found to be independent predictor of CIN development during multiple-factor regression analysis (29). The incidence of CIN (defined as increase in serum creatinine level by 25% or 0.5 mg/dl from baseline within 48 hours after angiography) increased from 10.3% (for the most high hematocrit quintile) to 23.3% (for the most low hematocrit quintile) (p for trend <0.0001).

Previous kidney transplantation

Concominant use of nephrotoxic drugs (e.g. cyclosporine) along with high incidence of diabetes and renal failure in patients who underwent kidney transplantation presents a contributory background for CIN development. Ahuja et al. (33) performed retrospective evaluation of contrast enhanced examination results in 144 patients with functioning renal allotransplantant. It was found that in general the incidence of CIN was 21.2% in the group and it was particularly high (42.8%) among those who were not hydrated before contrast enhanced examination.

The volume of administered contrast media

The amount of administered contrast media plays a primary role in development of CIN (28). This is the main modifiable CIN risk factor. However, the increased complicacy of coronary interventions inevitably results in increased volume of contrast agents used during procedure and therefore increases the risk of CIN. The correlation between the amount of administered contrast agent and increased incidence of CIN was observed in many studies (34, 35). According to McCullough et al. (5), the risk of CIN is minimal in patients receiving less than 100 ml of contrast medium.

Nephrotoxic drugs

It is considered that concomitant use of nephrotoxic drug and administration of contrast medium increases the risk of CIN development. Alamartine et al. reported the tendency to higher CIN rate (P = 0.07) in patients receiving nephrotoxic drug during angiography (including diuretics, non-steroidal anti-inflammatory drugs, drugs from “coxib’s” group, aminoglycosides, amphotericin B) (36). Therefore, according to established standards, nephrotoxic drug are discontinued (if it is possible) while performing contrast angiography in order to decrease the risk of acute renal impairment.

The role of angiotensin-converting enzyme inhibitors (ACEi) in modifying the risk of CIN development is still disputable. In the study performed by Kini et al. (19) the patients receiving ACEi at the time of contrast enhanced examination demonstrated more significant increase in serum creatinine level compared to patients not receiving ACEi. Similarly, in the study performed by Cirit et al. (37) the patients with chronic renal failure receiving ACEi demonstrated the higher incidence of CIN (15.6%) compared to patients not receiving ACEi (5.8%) after performing the contrast enhanced examination (P = 0.015). In contrast to data described above, the study performed by Dangas et al. demonstrated that relative risk of CIN after angiography in patients with chronic renal failure decreased when taking ACEi and comprised 0.61 (P = 0.005) (26). Likewise, the study performed by Gupta et al. (38) revealed that periprocedural use of IACF, captopril, decreased the risk of CIN development compared to control group.

The type of contrast media

Despite the structural similarity of currently used contrast agents (all of them are derivatives of benzoic acid) there are significant differences in chemical properties of these agents including the number of iodine molecules, sodium content and osmotic properties of the formulation. These properties specify such characteristics of contrast agents as osmotic concentration of solution, ionization degree and viscosity. The properties of contrast agents are listed in Table 2.

Up to now there have been many studies conducted comparing different contrast agents. Barrett et al. (39) in 1993 had already published the meta-analysis of 31 randomized studies in which the osmolarity of contrast agents was compared. The review included high-osmolar and low-osmolar contrast agents. The relative risk of increased serum creatinine level by more than 0.5 mg/dl after administration of low-

Table 2. The properties of contrast media .

Name	Osmolarity	Ionization
Diatrizoat	High-osmolar	Ionic monomer
Iotalamat	High-osmolar	Ionic monomer
Ioxitalamat	High-osmolar	Ionic monomer
Ioxaglat	Low-osmolar	Ionic dimmer
Iohexol	Low-osmolar	Non-ionic monomer
Iopamidol	Low-osmolar	Non-ionic monomer
Ioversol	Low-osmolar	Non-ionic monomer
Iopromide	Low-osmolar	Non-ionic monomer
Iobitridol	Low-osmolar	Non-ionic monomer
Iomeprol	Low-osmolar	Non-ionic monomer
Iodixanol	Izoosmolar	Non-ionic dimmer

osmolar contrast agents decreased to 0.61 (95% confidence interval, 0.48-0.77) compared to high-osmolar contrast agents.

The efficacy of low-osmolar contrast agents concerning the decrease of incidence of serum creatinine level elevation by more than 0.5 mg/dl was significant in patients with impaired renal function (RR 0.5, 95% CI 0.36ч0.68), but it was barely noticeable in patients with normal renal function (RR 0.75, 95% CI 0.52ч1.1). The investigators concluded that use of low-osmolar contrast agents may be useful in patients with existing renal pathology (39). These findings were confirmed in randomized multicenter study conducted by Rudnick A. et al. (21) comparing low-osmolarity nonionic contrast agent iohexol and high-osmolar ionic contrast agent diatrizoat in 1196 patients who underwent coronarography. The acute toxic renal impairment (increase in serum creatinine level by more than 1 mg/dl within 48 hours after the procedure) was observed in 7% of patients receiving diatrizoat compared to 3% of patients receiving iohexol ($P < 0.002$). The differences in nephrotoxicity between the two groups appeared only in patients with previous renal failure or renal failure associated with diabetes mellitus.

Poled analysis of 16 randomized controlled trials including 2727 patients compared the nephrotoxicity of iso-osmolar contrast agent iodixanol and toxicity of low-osmolar contrast agents (40). The peak of elevated creatinine level within 3 days after administration of contrast medium was significantly lower in patients receiving iodixanol and was 0.06 mg/dl compared to 0.10 mg/dl in other groups ($P < 0.001$). The CIN (defined as elevation of creatinine level by more than 0.5 mg/dl during 3 days after administration of contrast medium) was significantly rarer in patients receiving iodixanol (1.4% compared to 3.5% in other groups, $P < 0.001$). These differences in the incidence of CIN were even more evident in patients with chronic kidney disease (2.8% compared to 8.4% in other groups, $P < 0.001$) and in patients with diabetes mellitus and decreased renal function (3.5% compared to 15.5% in other groups, $P < 0.003$). In two studies, RECOVER (41) and ICON (42), patients with chronic kidney disease were randomized to receive iso-osmolar contrast agent iodixanol and low-osmolar contrast agent ioksaglat. The CIN development was defined as the increase in creatinine level by more than 25% or 0.5 mg/dl. The incidence of CIN in the RECOVER study was significantly lower in group of patients receiving iodixanol – 7.9% compared to 17.0% in ioksaglat group ($P = 0.021$), however, in ICON the tendency to lower the incidence of CIN did not achieved the level of significance (16.2% versus 24.2% in ioksaglat group, $P = 0.285$).

In general, the use of nonionic low-osmolar contrast agents leads to decrease in the incidence of CIN compared to high-osmolar contrast agents, especially in patients with chronic kidney disease and impaired renal function. The recent data shows that the use of iso-osmolar contrast agent iodixanol results in decreased frequency of elevated creatinine and reduces the CIN incidence compared to low-osmolar contrast agents which primarily pertains to patients with chronic kidney disease or concomitant diabetes mellitus and chronic kidney disease (41, 42).

Assessment of cumulative risk of CIN

Patients receiving contrast agents often have more than one CIN risk factors. Mehran et al. developed the CIN risk prognostic scale for patients undergoing percutaneous coronary interventions (31). The algorithm for risk estimation using Mehran scale is shown in Table 3.

Bartholomew et al. (43) proposed other risk estimation scale based on 8 variables related to CIN: creatinine clearance <60 ml/min, use of IABP, emergency coronary intervention, diabetes mellitus, congestive heart failure, hypertension, atherosclerosis of lower extremity vessels and volume of administered contrast agent.

Table 3. The scale of CIN risk following percutaneous coronary interventions (Mehran et al.). (31).

Risk factor	Index by scale
Hypotension	5
IABP use	5
Congestive heart failure	5
Age >75 years	4
Anemia	3
Diabetes mellitus	3
The volume of contrast agent	1 per each 100 ml
Creatinine level > 1.5 mg/dl	4
or	
GFR (by MDRD) of < 60 ml/min/1.73m^2	2 for GFR 40-60 4 for GFR 20-40 6 for GFR <20
	All indexes are summarized

Summarized index	CIN risk	Hemodialysis risk
5 or less	7.5%	0.04%
6-10	14.0%	0.12%
11-16	26.1%	1.09%
More than 16	57.3%	12.6%

IABP - intra-aortic balloon pump counterpulsation

THE PROGNOSIS FOR CONTRAST-INDUSED NEPHROPATHY

Presently CIN is the most common cause of acute renal failure (ARF) development in hospitalized patients. It leads to prolonged hospitalizations, increase in complication rate, mortality and treatment costs. Previous studies showed that invasive procedures with administration of contrast medium are a cause of ARF 12-24% of patients developing ARF during hospitalization (5, 44). Retrospective analysis in 16248 patients administered contrast medium showed that even low renal function deterioration may lead to significant increase in mortality independently of other risk factors, and also revealed that a slight increase in serum creatinine level, in fact, presents an apparent lowering of glomerular filtration rate (45). The in-hospital mortality was almost 5-fold higher in patients having CIN (34%) compared to patients without CIN (7%) (45). The prognosis was particularly poor in patients with history of renal disease in which contrast agent caused further decrease of renal function and also in dialysis patients (46). The in-hospital mortality in these groups were 14.9% and 27.5%, respectively, compared to 4.9% in patients after ARF with initially preserved renal function (46,47). According to the Registry of Mayo Clinic, the in-hospital mortality in patients who underwent PCI resulting in CIN development was 22% compared to 1.4% in patients without CIN (4). The in-hospital mortality was particularly high (36%) among patients required hemodialysis after administration of contrast medium (5).

During the first year after the administration of contrast medium the mortality rate in patients with chronic kidney disease existing before contrast enhanced examination remains very high. Mortality reaches 45.2% in hemodialysis patients group, 35.4% - in patients with decreased renal function and 19.4% in patients with preserved renal function (46). According to the Registry of Mayo Clinic, 1 year mortality after PCI directly correlates with creatinine clearance and is of 1.5% in patients with creatinine clearance less than 70 ml/min and 18.3% in patients with creatinine clearance less than 30 ml/min (48).

THE PROPHYLAXIS OF CONTRAST-INDUSED NEPHROPATHY

The measuring of baseline serum creatinine level should be performed before angiography in patients with history of chronic kidney disease, proteinuria, previous kidney surgery, diabetes mellitus, arterial hypertension or gout (49). Earlier the estimation of creatinine clearance (CC) was commonly performed, and many formulas were proposed for this purpose (50). The acceptable analytical method of CC estimation was Cockroft-Gault method (51). However, Cockroft-Gault formula (as well as other formulas for CC estimation) provides the estimated value in ml/min which should be additionally correlated to body surface area (using combined scales) in order to obtain the values in ml/min/1.73 m2 (52). In the MDRD study (Modification of Diet in Renal Disease Study) the formula for GFR estimation in ml/min/1.73 m2 was introduced and named with study abbreviation (53). Afterwards this formula was checked for validity regarding various patients groups (54). Therefore, presently the MDRD formula is recommended for use in majority of patients groups by international and Russian nephrological and cardiological societies (55, 56).

It should be remembered that the use of serum creatinine for GFR estimation implies the stable patients` condition; therefore the results will be unreliable if GFR level is changing rapidly, in particular, in acute renal failure. In such clinical situations (rapidly changing renal function, before the administration of nephrotoxic drugs) the Rehberg-Tareev test may provide the better evaluation of GFR compared to estimation methods. However, the Rehberg-Tareev test is very rarely used in routine cardiological practice. Thus, in case of CIN development it is not quite acceptable to use analytical (estimation) methods of GFR evaluation for process dynamics.

Nevertheless, before performing the angiography and administration of contrast medium, the patients with GFR of less than 60 ml/min/1.73 m2 should be revealed because they are the high risk patients concerning development of nephropathy. If only the diagnostic examination in patients with risk factors for CIN development is needed, one should consider the alternative methods of visualization not requiring the administration of contrast agent. Repeated measurement of serum creatinine level should be performed within 24 48 hours after the administration of contrast agent in the body.

The CIN prophylaxis is very important because of its extremely poor prognosis. Up to now, the several potential strategies of CIN risk reduction have been studied.

Hydration

There is a strict consensus between specialists stating that the adequate increase in circulating blood volume (CBV) before the administration of contrast agent is the main strategy of CIN prophylaxis despite the absence of previously conducted direct randomized controlled trials comparing the strategy of CBV increase and the strategy of preserved baseline CBV before the contrast administration. The several potential mechanisms may contribute to benefits of increased CBV including the dilution of contrast agents in tubular lumen, decrease of renin-angiotensin system activity due to increased sodium concentration excreted to distal nephrone, minimized impeding of renal nitric oxide production caused by contrast agents (25).

The positive effect of adequate hydration on decrease of the incidence of CIN was established in randomized study conducted by Solomon et al. (57). In 78 patients referred to coronarography, hydration with hypotonic NaCl solution (0.45%) 12 hours prior to and during 12 hours after contrast enhanced

examination led to better outcomes compared to use of combination of hypotonic NaCl solution (0.45%) with mannitol or use of combination of hypotonic NaCl solution (0.45%) with furosemide (57). The incidence of CIN in three groups comprised 11%, 28% and 40%, respectively (p=0.05). In randomized PRINCE study, the achievement of forced diuresis by intravenous administration of combination of hypotonic NaCl solution (0.45%) with mannitol and furosemide demonstrated the conservative benefit in CIN prevention compared to control (hypotonic NaCl solution and placebo) (58). Two randomized trials compared the different hydration methods: intravenous versus oral (59, 60). The first study conducted by Taylor et al. in 36 patients compared the 24-hour intravenous administration of hypotonic solution (0.45%) and oral intake of 1000 ml of liquid in combination with following 6-hour intravenous administration (59). While the study conducted by Taylor et al. did not show significant differences in the incidence of CIN (11.1% compared to 5.6% in respective arms) (59), the study conducted by Trivedi et al. including 53 patients demonstrated the benefit of intravenous administration of liquids (the incidence of CIN 3.7% compared to 34.6%, P = 0.005) (60). Two other small studies compared two infusion regimens before the use of contrast: infusion prolonged to 24 hours (including night-time) and short-term bolus infusion of liquids before catheterization (61, 62). The first study demonstrated significant impairment of renal function and greater decrease of GFR in the group with bolus liquids infusion (delta GFR 34.6 ± 25.7 ml/min/1.73 m2 compared to night infusion group – delta GFR 18.3 ± 25.0 ml/min/1.73 m2, P < 0.05) (61), while the second study did not reveal the significant differences between two infusion regimens (62).

Open-labeled, randomized trial conducted by Mueller et al. (63) raised question concerning the concentrations of liquids to infuse while performing hydration for CIN prophylaxis. Comparison of isotonic NaCl solution (0.9%) with hypotonic NaCl solution (0.45%) in a total of 1620 patients who underwent percutaneous coronary intervention demonstrated the benefit of isotonic solution in decreasing the incidence of CIN (0.7% compared to 2% in other group, P = 0.04) (63). The benefits of isotonic NaCl solution were especially noticeable in women with diabetes mellitus and in patients who received more than 250 ml of contrast agents (63). The better efficacy of isotonic NaCl solution compared to hypotonic solution can be explained by its stronger capacity to increase CBV. Prospective, single centre, randomized trial conducted by Merten et al. (64) in 119 patients revealed the benefits of hydration with isotonic sodium bicarbonate solution (154 mEq/l) 1 hour before administration of contrast medium and during 6 hours after administration of contrast agent iopamidol compared to hydration with isotonic NaCl solution (the incidence of CIN was 1.7% compared to 13.6%, P = 0.02). If speculate, it can be supposed that alkaline urine decreases the nephrotoxicity of iodine-containing contrast media due to shift in oxidation reduction potential or due to decreased contrast viscosity in rectal vessels. As this study had relatively small population and the majority of patients were not included in long-term follow-up, it is reasonable to conduct larger randomized multicenter study in order to better evaluate the efficacy of this simple and inexpensive method of CIN prophylaxis.

The CIN Working Panel published the Consensus in American Journal of Cardiology (65). After the careful reevaluation of available information regarding performed studies, this group offered the hydration regimen in order to increase the CBV using isotonic crystalloids (1.0-1.5 ml/kg/hour) within 3-12 hours before the contrast enhanced examination and infusion continuation up to 6-24 hours for prevention of CIN in patients with risk factors (65). However, such a load should be prescribed very carefully in patients with chronic heart failure (CHF). In case of CHF the greater benefit may be achieved by stabilization of patient`s hemodynamics compared to excessive hydration.

Acetylcysteine

The use of Acetylcysteine as an agent with antioxidant properties in prophylaxis of CIN is based on the assumption that CIN is caused by active oxygen forms resulting from direct toxic effect of contrast media on tubular epithelium. In randomized placebo-controlled study conducted by Tepel et al. 83 patients with initially increased serum creatinine received prophylaxis in the form of hydration or hydration combined with Acetylcysteine before contrast agent administration (66). It was found that hydration combined with Acetylcysteine is only superior to hydration in terms of decreasing the incidence of CIN (2% compared to 21% in only hydration group, P = 0.01). These results were accepted with enthusiasm and Acetylcysteine was accepted in many clinics as a standard in prophylaxis before contrast enhanced examinations, especially in patients with risk factors for CIN. Afterwards, the preventive properties of Acetylcysteine were confirmed in the study “The Acetylcysteine to Prevent Angiography-Related Renal Tissue” (67), in which 54 patients demonstrated better results with Acetylcysteine compared to placebo in decreasing the incidence of CIN (8% compared to 45%, P = 0.005).

Later, the optimism regarding the efficacy of Acetylcysteine weakened because several further studies (68, 69, 70, 71, 72, 73) did not show significant benefits of Acetylcysteine compared to control groups (Table 4). Since the use of standard doses of Acetylcysteine (600 mg bid orally) did not result in anticipated decrease of the incidence of CIN, some researchers started to use the higher doses of Acetylcysteine. In the study conducted by Briguori et al. (74) including patients with chronic kidney disease the comparison of standard (600 mg) and high (1200 mg) oral doses of Acetylcysteine bid before contrast enhanced examination was performed. It was found that the incidence of CIN was

Table 4. The role of Acetylcysteine in CIN prevention after coronarography.

Study, (reference)	N	Inclusion criteria	ACC dose in the study group $			Definition of CIN	CIN rate (%)		P
			Day 1	Day 0	Day 1		ACC	Control	
Azmus (69)	397	Cr ⩾ 1.3 mg/dl, DM or age ⩾ 70 years	600 mg bid	600 mg bid	600 mg	Cr elevation by ⩾ 25% or ⩾ 0.5 mg/dl within 48 hours	7.1	8.4	0.62
Boccalandro (70)	179	Cr > 1.2 mg/dl or CC < 50 ml/min	600 mg bid	600 mg bid		Cr elevation by ⩾ 0.5 mg/dl within 48 hours	13	12	0.84
Briguori (71)	183	Cr > 1.2 mg/dl and/or CC < 70 ml/min	600 mg bid	600 mg bid		Cr elevation by ⩾ 25% within 48 hours	6.5	11	0.22
Kay (72)	200	Cr >1.2 mg/dl and/or CC < 60 ml/min	600 mg bid	600 mg bid		Cr elevation by ⩾ 25% within 48 hours	4	12	0.03
Marenzi (68)	354	STEMI	600 mg bid or double dose at once	600 mg bid or double dose at once	600 mg bid or double dose at once	Cr elevation by ⩾ 25% within 72 hours	15 versus 8*	30	<0.001
Webb (73)	487	GFR of < 50 ml/min/1.73 m^2		500 mg intravenously		GFR decrease by >5 ml/min/1.73 m^2	23.3	20.7	0.57

ACC – Acetylcysteine; Cr - serum creatinine; CC - creatinine clearance;
GFR - glomerular filtration rate; DM - diabetes mellitus; STEMI - ST-segment elevation myocardial infarction;
$ - oral ACC if not other indicated;
* - three study groups: standard dose versus double dose versus placebo.

significantly lower in group of patients receiving high doses (4% compared to 11%, P = 0.03). The benefits of high Acetylcysteine dose were even more apparent in patients received the large volume of contrast agent (more than 140 ml). In the study "Rapid Protocol for the Prevention of Contrast-Induced Renal Dysfunction" (75) patients with moderate or significant renal dysfunction selected for specified percutaneous coronary interventions received intravenous Acetylcysteine before the intervention (at a dose of 150 mg/kg) and after the intervention (50 mg/kg). Compared to control group, the group or "fast prophylaxis" demonstrated the lower the incidence of CIN (5% versus 21% in control group, P = 0.04).

The meta-analyses of the studies conducted with Acetylcysteine had summarized (76, 77) that Acetylcysteine may reduce the incidence of CIN, however, the studies were very heterogeneous in terms of their design, and the results were inconsistent. Therefore, we should anticipate the new investigations which would specify the therapy duration, drug doses and the route of Acetylcysteine administration.

Dopamine

Given the dilation effect of dopamine on renal vessels and its ability to increase the renal blood flow, this drug is potentially useful as preventive agent for CIN prophylaxis. This hypothesis was evaluated in several studies, but the results were found to be controversial. While in one study (78) dopamine decreased the elevation of serum creatinine level after administration of contrast media, in other studies this effect of dopamine was not noticeable at all (79) or appeared only in patients with baseline serum creatinine level of 2.0 mg/dl (80). Moreover, in patients with peripheral arteries impairment who developed CIN after contrast enhanced examination, the negative effect of dopamine was reported (78,81).

Fenoldopam

Postsynaptic dopamine receptors refer to GPCR receptors class associated with G protein (G protein-coupled receptors), also known as semispiral receptors. There are at least 5 different subtypes of dopamine receptors D1-5. Receptors D1 and D5 share the significant homology and are associated with GS protein which stimulates adenylatcyclase, therefore they are usually considered as D1-like receptors. Other receptors in this subclass are similar to D2 and are associated with Gi protein which inhibits adenylatcyclase; therefore, they are collectively referred to as D2-like receptors.

Fenoldopam is a selective antagonist of postsynaptic D1-like receptors and cause both systemic and renal arterial vasodilatation. Therefore, its use does not deteriorate the renal perfusion despite the lowering of systemic BP. In experiments on animal fenoldopam demonstrated its ability to counter the reduction of renal perfusion and decrease of GFR after administration of contrast media (82). Observational studies demonstrated the low the incidence of CIN in high-risk patients while using fenoldopam (19, 83, 84). In randomized, double-blind, placebo-controlled study the use of combination of fenoldopam with hydration compared to hydration alone led to increased renal blood flow with decreased serum creatinine level within 72 hours after contrast enhanced examination and to a tendency to decrease in the incidence of CIN (21% compared to 41%, respectively; P = 0.14) (85). Two other prospective randomized trials showed the opposite (negative) results (86, 87). In the first study (86) the patients received only hydration with hypotonic NaCl solution (control) for CIN prophylaxis or the combination of hypotonic NaCl solution with fenoldopam (at a dose of 0.1 μg/kg/min within 4 hours before and 4 hours after contrast enhanced examination); the third group received Acetylcysteine. The incidence of CIN was found similar in fenoldopam and control groups (15.7% versus 15.3%, respectively). The second large study conducted by Stone et al. (87) confirmed the absence of fenoldopam superiority. In this double-blinded study 315 patients (in total) were randomized to receive fenoldopam (0.05 μg/kg/min with dose titration up to 0.1 μg/kg/min) or placebo on the background of hydration with hypotonic NaCl solution (0.45%). Fenoldopam (or placebo) administration was started 1 hour before the procedure and

during 12 hours after its termination. The study did not show significant differences in the incidence of CIN evaluated during up to 96 hours after the procedure (33.6% in fenoldopam group versus 30.1% in control group), as well as the difference in rate of haemodialysis, repeated hospitalizations and lethality within up to 30 days (87).

Terstein et al. supposed that insufficient effect might be the consequence of previous studies inability to choose the dose of fenoldopam effective for kidneys. They offered to administer fenoldopam directly to the renal arteries via bifurcated renal infusion catheter. In randomized study designed by Terstein et al. (88) the patients referred to coronary angiography received intravenous fenoldopam first according to cross-over design, and after the washout period they started to receive fenoldopam intrarenally. Compared to intravenous fenoldopam administration, its intrarenal use was associated with significantly higher GFR (73.7 ± 3.1 ml/min versus 62.6 ± 2.5 ml/min, respectively; P = 0.0007). It was noted that fenoldopam level in plasma was significantly lower after intrarenal use (3.3 ± 0.3 vs 4.8 ± 0.3 ng/ml, respectively; P <0.0001), as well as major adverse events and systemic hypotension occurred with lower frequency (systolic BP 125.5 ± 3.6 mmHg vs 117.4 ± 2.8 mmHg; P <0.0001).

Theophylline

As mentioned previously, several studies showed the role of adenosine in negative response of renal hemodynamics to administration of contrast substances (89, 90). This was the basis for hypothesis that antagonist of adenosine A1 receptors, theophylline, may prevent the contrast-induced decrease of renal perfusion and GFR. Several randomized studies were conducted, but the results were found controversial. In the study conducted by Briguori et al. (91) the prophylactic intravenous administration of theophylline (200 mg) decreased the incidence of CIN in patients with chronic kidney disease compared to placebo (4% versus 16%, respectively, P = 0.046). In other study conducted by Kapoor et al. (92) 70 patients with diabetes mellitus were randomized into two groups. The first group received 200 mg of theophylline intravenously before coronarography twice a day and continued to receive it during 48 hours after angiography, and the second group received only placebo. No patients among those who received theophylline developed the increase in serum creatinine level more than by 25% from baseline compared to 20% in control group (P = 0.017). the incidence of CIN, determined in this study as decrease of GFR more than by 25%, was significantly lower in theophylline group (3% versus 31% in control group; P = 0.004). Another randomized placebo-controlled study conducted by Kolonko et al. showed the benefits of intravenous dose 165 mg of theophylline compared to placebo concerning the inhibition of GFR lowering, as well as concerning the plasma erythropoietin level and rennin activity (93). However, two other studies did not show the benefits of theophylline compared to placebo in CIN prophylaxis (81,89).

Calcium channel antagonists

Earlier, the data on changing the calcium metabolism after administration of contrast medium in the body and on calcium channel antagonists ability to decrease vasospasm was received. Based on this, the several studies were initiated investigating the calcium channel antagonists impact on CIN development. In small randomized study in 35 patients the GFR did not decrease after administration of calcium channel antagonist nitrendipine though it significantly decreased in patients received placebo (27% at day 2 after the contrast enhanced examination, P < 0.01) (95). In contrast to these data, in two other studies with calcium channel antagonists, nitrendipine and nifedipine, there was no significant difference between study and control groups in the change in serum creatinine level over time (96, 97).

Prostaglandin E1

It is known that prostaglandins levels decrease in case of CIN development. These data triggered the evaluation of the preventive role of intravenous prostaglandin E1 in CIN prophylaxis (98). In randomized, double-blind, placebo-controlled study the efficacy of three different doses of intravenous prostaglandin E1 was investigated. All patients groups received prostaglandin E1 regardless to its dose showed significantly lower increase in serum creatinine level after the contrast enhanced examination compared to placebo. The most prominent effect was observed in the group of patients received the moderate (intermediate) prostaglandin dose (20 ng/kg/min) (98).

Ascorbic acid

The possible role of oxidant stress and free radicals formation in CIN pathogenesis was the basis for evaluation of ascorbic acid as preventive measure. In randomized, double-blind, placebo-controlled study the oral intake of ascorbic acid (3 g before contrast enhanced examination and 2 g twice after contrast enhanced examination) was evaluated in 231 patients who underwent cardiac catheterization (99). The CIN was defined as the increase in serum creatinine level of 0.5 mg/dl or 25%. The incidence of CIN was significantly lower in group of patients received ascorbic acid (9% compared to 20% in control group, P = 0.02).

Atrial natriuretic peptide

The evaluation of atrial natriuretic peptide (ANP) role if administered at three different doses in randomized placebo-controlled study designed by Kurnik et al. did not reveal ANP capacity to prevent CIN.

Hemodialysis and hemofiltration

In patients with renal dysfunction the several studies were conducted investigating the efficacy of

hemodialysis performed immediately after contrast enhanced examinations in order to prevent further renal function deterioration. These studies showed the similar results suggesting that hemodialysis does not decrease the incidence of CIN if used for prophylaxis (100,101).

Two studies conducted by Marenzi A. et al. (102,103) investigated the efficacy of continuous hemofiltration for CIN prevention in patients with severe chronic renal failure (serum creatinine >2 mg/dl) compared to intravenous hydration. In the hemofiltration group the incidence of CIN (elevation of creatinine level by more than 25%) was significantly lower (5% versus 50%, respectively; P <0.001), as well as in-hospital mortality (2% versus 14%, respectively; P = 0.02). However, since the direct aim of hemofiltration is a decrease of serum creatinine level, the interpretation of these studies results concerning hemofiltration benefits based on this criterion is quite disputable. Thos method requires further evaluation. Among all mechanisms involved in process of continuous hemofiltration, the controlled hydration using significant volume before contrast enhanced examination probably plays the crucial role (102).

Nephrotoxic drugs discontinuation and metformin

As mentioned previously, the potentially dangerous nephrotoxic drugs must be discontinued before the contrast enhanced examination in patients with known risk for CIN development. The metformin discontinuation before the contrast enhanced examination is also a part of general clinical practice as the risk of metabolic acidosis increases significantly if renal function worsening is observed after the contrast enhanced examination.

CONCLUSION

Contrast-induced nephropathy is an iatrogenic pathology occurring after the administration of contrast media in the body. The contrast-induced direct cytotoxic effect on renal tissue along with decrease of renal perfusion is the most obvious pathway of CIN pathogenesis, while other mechanisms are poorly investigated. Though CIN occurs rather rarely in general population of patients who underwent contrast enhanced examination, it develops in significant number of patients with existing renal pathology, diabetes mellitus and in older patients. The probability of development of acute renal impairment after administration of contrast media is significantly more in presence of several CIN risk factors. Presently, the best strategy of CIN prophylaxis is a detection of patients with risk factors and performing an adequate periprocedural hydration. The role of various drugs in CIN prophylaxis is still disputable and requires further investigation. Despite the remaining controversy concerning the nephrotoxicity of various contrast agents, the iso-osmolar and low-osmolar contrast agents are to be used in modern clinical practice for CIN prophylaxis, though high-osmolar contrast media should be strictly avoided in patients with impaired renal function.

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Information report. Annual Scientific and Practical Conference of Russian Scientific Society of Interventional Cardioangiology "Theory and Practice of Interventional Cardioangiology"

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Annual Scientific and Practical Conference of Russian Scientific Society of Interventional Cardioangiology "Theory and Practice of Interventional Cardioangiology" took place on November 11-13, 2009. The Conference has been held in the Engineering building of the State Tretyakov Gallery and, according to the tradition, plenary sessions were accompanied by live transmissions from the Center of Endosurgery and Lithotripsy (CELT) and Moscow City Center of Interventional Cardioangiology (MCCIC).

The Conference has one distinctive feature – it was attended only by Russian specialists. The geography of participation was quite large – from the Far East to the European territory, from the North to the South of Russia. All those who wanted to make their presentations or participate in discussions could do it - young interventionists, as well as their eminent colleagues. Two Moscow centers – CELT and MCCIC – warmly welcomed the operators from other Russian clinics. It is safe to say, that this three-days Conference was a full-measure reflection of the state of interventional cardiology and angiology in Russian Federation.

The opening ceremony started by the words of welcome by the president of RSSIC Zaza Kavteladze. He emphasized the importance of the event and ended his bright and emotional address by the citation from Bulat Okudjava's song calling his colleagues to collaboration, creation and consent. The President of CELT A. Bronstein and the Director of MCCIC, the founder of Russian Society of Interventional Cardioangiology D. Iosseliani welcomed the participants after him. Both of them stressed the point that, with the account of the prevalence and the significance of cardiovascular diseases, modern approaches to the treatment and the prevention of these diseases remain vital, and for these reasons the Conference is timely and highly necessary.

After that, the president of RSSIC Zaza Kavteladze addressed the participants for the second time. He shortly reminded them of the main stages of RSSIC activities during the reporting period and made a special point of the novelties being suggested at the Conference. In particular, he mentioned the upgrading of the website of the Society, its active completion with informational and news content. During the preparatory period of the Conference the website became a necessary interactive resource which helped to get preliminary registration, to present specific wishes and to prepare individual programs. Besides, for the first time each speaker, moderator or member of the panel received detailed instructions concerning the order of sessions and discussions. For the first time in Russian practice it became possible to suggest and to implement a strict control of time-limit for presentations using a computerized system. The efforts of RSSIC led to the approval of the specialty - Endovascular Therapy and Diagnostics – by the Ministry of Health Care and Social Development. Together with the representatives of medical industry the Society has elaborated and realized in practice several educational programs for physicians. Much more is off to be done in the nearest future. It concerns the training of young specialists, the skills upgrading of practicing interventionalists, the propagation of information on cardiovascular diseases among the population. The President emphasized that the Society plans to publish the learning programs and resources, available for all specialists. For this purpose within the next 2 years, before the next Congress of RSSIC in 2011, seven issue related scientific and practical conferences on different problems of interventional cardiology, angiology and radiology will be held.

The first session chaired by Z. Kavteladze (presidium members S. Abugov, A. Arablinsky, V. Demin, I. Zyrianov, V. Ivanov, D. Iosseliani and A. Fedorchenko) was dedicated to the fundamental diagnostic studies. Zaza Kavteladze opened the first "How I Do It" session dedicated to the

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study of the coronary arteries. The speaker V. Glagolev (CELT, Moscow) described in details the possibilities and the disadvantages of modern MSCT-coronary angiography and demonstrated comparative possibilities of invasive and non-invasive coronary angiography. During the first live tramsmission from MCCIC the operators A. Samko (Russian Cardiological Center, Moscow) and A. Koledinsky (MCCIC, Moscow) have demonstrated coronary angiography from the femoral approach while emphasizing and discussing all its peculiarities for maximally accurate and high-quality visualization of the coronary lesions. This was followed by live transmission from CELT with the demonstration of coronary angiography from the radial approach, with the discussion of the particularities of this approach. The presentations by P. Pavlov (Regional clinical hospital, Khanty-Mansisk) and V. Artemiev (Center of Heart Surgery "CorAll", Nijny Novgorod) also dealt with "out-patient" coronary angiography with the use of radial approach. It was emphasized, that the rare use of the interventions through the radial approach in our country is unjustified. Yu. Artamonova (CALT, Moscow) presented the results of the randomized trial comparing the radial and the femoral approaches using a suturing device. It was shown that these approaches are equal in their safety, whole each of them has certain advantages, and the choice of the approach must be based on clinical indications.

The results of randomized trials and their significance for clinical practice were discussed during the second session. The session's moderator Z. Kavteladze and the members of the presidium (S. Abugov, A. Babunashvili, V. Ganiukov, D. Iosseliani, V. Kucherov, A. Osiev, I. Pershukov, V. Chestukhin) listened to a detailed analysis of the most important recent randomized trials aimed at the comparison of surgical, endovascular and medical methods of treatment of the coronary heart disease, such as «COURAGE» and «SYNTAX». These trials were the subject of the analytical reviews made by S. Abugov (Petrovsky Scientific center of Surgery, Moscow) and I. Pershukov (Regional clinical hospital N1, Voronezh). V. Ivanov from the 3rd Vishnevsky Central Military Clinical hospital (Krasnogorsk, the Moscow region) reported the long-term follow-up of the selective tactics of stenting of "borderline" coronary stenoses. D. Gromov (MCCIC, Moscow), V. Ganiukov (Research Institute for the Complex Problems of Cardiovascular Diseases, Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo), A. Krylov (Research Institute of Cardiology, Tomsk) discussed the unsolved problems of the treatment of multi-vessel coronary disease. The choice of drug-eluting stent for everyday clinical practice on the base of in vitro testing of different stents was the subject of presentation made by E. Merkulov (Russian Cardiological Center, Moscow). Interesting data on the frequency and the causes of coronary stent thromboses were presented by N. Semigolovsky from the Clinical Hospital N 122 named after Sokolov (St.Petersburg).

The sessions NN 3 and 5, also held under the heading "How I Do It" during the first day of the Conference, focused on the problems of angiography of major lower limb arteries, extra- and intracranial cerebral vessels. Their moderators Z. Kavteladze and V. Demin, as well as presidium members S. Zakharov, I. Eroshkin, S. Kapranov, D. Ovcharenko, E. Chebotar, E. Belozerov, S. Terekhin, V. Shipovsky, S. Yakovlev listened to the communications on MRT angiography, MSCT major lower limb arteries, extra- and intracranial cerebral vessels presented by V. Sinitzyn (Therapeutic and Rehabilitation Center, Moscow), V. Glagolev (CELT, Moscow). The presentation of D. Salnikov (Central Clinical Hospital of the Presidential Administration, Moscow) was dedicated to three-dimensional rotation angiography.

These sessions included several live transmissions from two Moscow centers with the demonstration of angiography of major lower limb arteries from the radial approach (operator K. Bylov, CELT, Moscow) and the femoral approach (transmission from MCCIC, operator V. Shipovsky, City clinical hospital N57, Moscow). S. Protzky (С.В. Процкий (Scientific Center of neurology, Moscow) demonstrated to the audience the procedure of angiography of extra- and intracranial cerebral vessels.

The whole session № 4 was dedicated to the TASC 2007 Guidelines and their realization in everyday clinical practice. Session's moderator Z.Kavteladze and presidium members V. Demin, I. Eroshkin, S. Zakharov, S. Kapranov, L. Kokov, D. Ovcharenko, V. Shipovsky listened to the interesting presentations of Z. Kavteladze (CELT, Moscow) and S. Kapranov (RSMU, Moscow) on angioplasty and atherectomy for iliac and femoral arterial lesions and discussed them. V. Demin from Orenburg Regional Clinical hospital presented challenging data on the use of intravascular ultrasound study and antiembolic filters for the angioplasty of superficial femoral artery. K. Bylov (CELT, Moscow) spoke of the first Russian trial of a drug-eluting stent use for the angioplasty or peripheral arteries. The session ended with an animated discussion. It was noted that despite a rather long history, endovascular surgery of peripheral arteries is quick-stepping to new achievements and is continuously refilled with new devices and technologies.

A large plenary session chaired by David Iosseliani was dedicated to endovascular treatment of acute myocardial infarction and acute coronary syndrome. The members of presidium V. Ganiukob, S. Kozlov, A. Krylov, V. Mazaev, A. Samko, V. Sukhov, V. Shpektor spoke about the most thrilling problems of the treatment of AMI. In his opening presentation "Endovascular treatment of AMI" D. Iosseliani spoke of modern methods of treatment of acute myocardial infarction.

He emphasized that mechanical revascularization within the first hours after the onset of the disease is the best method of treatment. This is confirmed by the experience of the leading Russian and Western clinics. However there are many aspects and techniques of treatment which could improve the results. Among them are thrombus extraction and non-pharmacological methods of thrombus destruction. Thrombolythic therapy is also a method of continuing relevance. At present the difficulties related to timely diagnostics and transportation of patients do not allow to perform angioplasty in all patients during the acute stage of myocardial infarction, so thrombolythic therapy, being the most available method of myocardial reperfusion, is carried out in the majority of cases during this stage. Very often interventional cardiologists face the patients who received thrombolythic therapy at pre-hospital or early in-hospital stage. The particularities of endovascular interventions in cardiogenic shock were addressed in the presentation of A. Shpektor (Faculty of post-graduate education, State Medical and Stomatological University, Moscow). V. Ivanov from the 3rd Vishnevsky Central Military Clinical hospital (Krasnogorsk, the Moscow region) evaluated the effectiveness and the safety of different devices for thrombus aspiration in acute coronary occlusions. The first experience with the use of «MGUARD» stents with net coating for the prevention of distal embolism was reported by T. Kislikhin (Regional clinical cardiological dispensary, Samara). The analysis of the epidemiology of AMI-related mortality depending on the availability of high-technology methods of treatment was given in the presentation of N. Mikhalchikova (Almazov Federal Center of Heart, Blood and Endocrinology, St. Petersburg) on the base of the registry of acute myocardial infarction in St. Petersburg. S. Zhernakov (Railroad Clinical Hospital, Samara, Medical Unit of the JSC "Tatneft", Almetievsk) shared his experience with interventional myocardial revascularization in acute myocardial infarction. The presentation of A. Melnikov (Center of Intensive Cardiology and Cardiovascular Surgery, Krasnoyarsk) was dedicated to the complications of coronary angioplasty in myocardial infarction. The specialists from Research Institute of Complex Problems of Cardiovascular Diseases presented comparative analysis of the results of treatment of acute coronary syndrome in Kemerovo and the European centers. V. Kulikovsky imparted the experience of Belgorod regional Clinical Hospital with the treatment of acute coronary syndrome in 2007–2009. A. Koledinsky (MCCIC, Moscow) made an intriguing presentation "Is Thrombus Extraction from the Infarct-related Artery for the Treatment of Acute Myocardial Infarction an Effective or Just a Spectacular Procedure?". The same subject – the use of catheter thrombus aspiration prior to percutaneous coronary interventions in STEMI – was addressed in the presentation of S. Kozlov from Yekaterinburg. D. Sazhnov (Clinical Hospital №3, Saratov) presented the analysis of the outcomes of percutaneous coronary interventions in patients with acute coronary syndrome. The specialists from Ivanovo Regional Clinical Hospital described an interesting technique of adaptation reperfusion during interventions for the treatment of acute myocardial infarction. S. Semitko from City Clinical Hospital N 81 (Moscow) discussed the results of the study of «no-reflow» phenomenon using optical coherent tomography. Pre-hospital systemic thrombolysis combined with the angioplasty of infarct-related artery in different terms fo in-hospital treatment of acute myocardial infarction was discussed in the presentation of I. Kovalchuk (MCCIC, Moscow).

In his closing address the session's moderator D. Iosseliani expanded on the key moments of presentations, and gave a modern viewpoint on the problem. He emphasized that toady the main efforts should be directed towards the optimization of the techniques of treatment and the improvement of the organization of medical care for patients with acute myocardial infarction.

I. Zyrianov opened the second day of the Conference by introducing the members of presidium A. Babunashvili, V. Ganiukov, V. Ivanov, D. Iosseliani, A. Osiev, A. Savchenko, V. Sukhov, V. Chestukhin. The morning session was dedicated to the thrilling problems of percutaneous interventions for the lesions of the left main coronary artery, bifurcation and ostial coronary lesions.

A. Babunashvili presented the unique experience of Moscow CELT clinic with the treatment of the lesions of the left main coronary artery, bifurcation and ostial lesions. The first presentation partially answered the question raised by the second speaker, V. Ganiukov: is there a scientifically validated algorithm of treatment in ostial lesion of the LAD? The problems of percutaneous coronary angioplasty and stenting for the lesions of the left main coronary artery and bifurcation lesions were addressed in the presentations of Z. Shugushev, V. Ivanov (3rd Vishnevsky Central Military Clinical hospital,Krasnogorsk, the Moscow region), I. Zyrioanov (Cardiological Center, Tiumen), V. Chestukhin (Shumakov Center of Transplantology and Artificial Organs , Moscow), A. Savchenko (Russian Center of Cardiology, Moscow). V. Demin (Regional Clinical Hospital, Orenburg) presented his experience with the use of drug-covered balloons for the treatment of in-stent restenoses. After an animated discussion on the session subject the audience assisted to a live transmission of endovascular interventions from CELT and MCCIC.

The next session was dedicated to angioplasty of the renal arteries (moderator V. Demin, presidium members Z. Kavteladze, A. Karev, L. Kokov, A. Krylov, E. Morozov, M. Poliak, S. Chernyshev).

Z. Kavteladze (CELT, Moscow) made a detailed review of indications for the angioplasty of the renal

arteries. In his presentation he noted that world experience suggests the necessity of a more balanced approach to the interventions on the renal arteries. In interesting presentation of A. Karev (Academician Pavlov State Medical University, Str. Petersburg) addressed the experience of endovascular treatment of chronic occlusions in bilateral lesions of the renal arteries. Renal arterial angioplasty and endovascular treatment of vasorenal hypertension were discussed in details by I. Kokov (Vishnevsky Institute of Surgery, Moscow) and S. Chernyshev (Regional clinical Hospital № 1, Yekaterinburg). According to the tradition, the session ended by a discussion with the participation of the moderator and the members of presidium.

The session dedicated to endovascular surgery of extra- and intracranial cerebral arteries opened at noon on November 12. The moderator A. Fedorchenko and the representative presidium (T. Kislukhin, A. Maltzev, M. Maliukov, L. Marchenkov, S. Protzky, S. Yakovlev) actively participated in the discussion of indications and contraindications for the stenting of internal carotid arteries (presentation of Z. Kavteladze with live transmission from CELT. Moscow), endovascular treatment of patients with stenotic lesions of two and more brachiocephalic arteries, endovascular surgery of intracranial cerebral vessels' aneurysms (speaker A. Fedorchenko, Ochapovsky Regional Clinical Hospital №1, Krasnodar), stenting of internal carotid arteries. S. Protzky (Scientific Center of Neurology, Moscow) spoke of interventional methods of treatment of ischemic brain disease, while S. Yakovlev (Burdenko Research Institute of Neurosurgery, Moscow) described endovascular surgery for carotid arterial lesions. The work of V. Rudman (Regional Clinical Hospital № 2, Khabarovsk) dealt with the effectiveness of endovascular treatment of arterial aneurysms. A useful experience with endovascular treatment of subclavian arterial pathology was presented by D. Perukhin (State Medical and Stomatological University, Moscow) and A. Ivanov (Polenov Russian Research Institute of Neurosurgery, St. Petersburg) who described the principles of venous system response to the changes of cerebral outflow. The session included live transmission of endovascular interventions from CELT and MCCIC and was ended by a discussion with active participation of presidium members and attendees of the conference.

A burning problem – prevention and treatment of contrast-induced nephropathy – was in the focus of attention of the next plenary session (moderator V. Ganiukov, presidium members D. Dundua, A. Eroshenko, M. Kaputin, L. Marchenkov, I. Pershukov, E. Sharabriin). D. Dundua from CELT (Moscow) presented the analysis of the newest data and his own studies on the prevention of contrast-induced nephropathy. I. Pershukov (Regional Clinical Hospital №1, Voronezh) gave a detailed review of the role of creatinine clearance in long-term of the outcomes of coronary stenting. The presentation of a research group from Sechenov Medical Academy (Moscow) was dedicated to the choice of the contrast medium. During the discussion it was noted that current contrast media are rather safe for being used in everyday practice of interventional cardiology and angiology, however, it is necessary to undertake measures for the prevention of nephropathy in order to decrease the risk of renal failure development.

Z. Kavteladze chaired the following session dedicated to endografting of thoracic and abdominal aortic aneurysms. Presidium members – S. Abugov, A. Karev, O. Karakulov, A. Osiev, A. Orlov, A. Troitzky, S. Chernyshev – and the attendees listened to the presentations of Z. Kavteladze (CELT, Moscow), S. Abugov (Petrovsky Scientific Center of Surgery, Moscow), A. Osiev (Meshalkin Research Institute of Circulation Pathology, Novosibirsk), S. Chernyshev (Regional Clinical Hospital №1 , Yekaterinburg), A. Karev (Pavlov State Medical University, St. Petersburg), M. Generalov (Russian Scientific Center of Radiology and Surgical Technologies, St. Petersburg). The speakers pointed out that modern stent-grafts and continuous perfection of surgical technique allow for successful performance of endografting in the most severely ill patients with thoracic and abdominal aortic aneurysms and iliac arterial aneurysms. The technique of endografting becomes the method of choice in patients with severe associated pathology and successfully replace surgical therapy. Two live transmissions from CELT showing bifurcation endografting of abdominal aortic aneurysms using different stent-grafts (operator Z. Kavteladze) were a bright illustration for these reports.

The final day of the Conference started with a plenary session dedicated to angioplasty of chronic coronary occlusions. It was chaired by A. Babunashvili, and V. Demin, V. Ivanov, D. Iosseliani, L. Kasianov, A. Samko, A. Osiev, S. Piskunov and A. Fedorchenko were presidium members.

In his presentation A. Babunashvili (CELT, Moscow) noted that the success of recanalization of coronary occlusions depends on the skills, the technique and the insistence of the operator. Frequently only second and third attempts of antegrade recanalization as well as retrograde recanalization technique allow to achieve success in most cases, where until recently surgical revascularization was inevitable. The problem of retrograde recanalization of chronic occlusions was addressed also in the presentation of A. Osiev (Meshalkin Research Institute of Circulation Pathology,. Novosibirsk), who spoke of several technical aspects of retrograde technique use. The speakers from MCCIC and the department of endovascular surgery of Russian Center of Cardiology also discussed th problem of recanalization of chronic occlusions of the coronary arteries. V. Demin (Regional City Hospital, Orenburg)

shared his experience with endovascular therapy for chronic coronary occlusions. An interesting discussion closing the session was supplemented by live transmissions from two Moscow centers – CELT and MCCIC.

The next session "Endovascular treatment of heart defects" was chaired by A. Osiev, with T. Kislukhin, L. Kokov, A. Orlov, V. Plekhanov, M. Puretzky, V. Sukhov, A. Khamidullin as presidium members.

V. Ganiukov (Research Institute for the Complex Problems of Cardiovascular Diseases, Kemerovo) presented four-years experience with endovascular closure of septal heart defects and patent ductus arteriosus using AMPLATZER occluders. A. Osiev (Meshalkin Research Institute of Circulation Pathology,. Novosibirsk(shared his experience with pulmonary valvuloplasty for isolated pulmonary arterial stenosis. The problems of safety and effectiveness of balloon atrioseptostomy performed in the settings of intensive care ward under EchoCG control were addressed in the presentation of T. Kislukhin (Regional Clinical Cardiological Dispensary, Samara). Transcatheter methods of congenital heart defects correction were discussed in the report presented by the authors from Ivanovo Regional Clinical Hospital. Immediate and long-term results of the closure of ASD-II using AMPLATZER devices were presented by M. Puretzky (Petrovsky Russian Scientific Center of Surgery, Moscow).

The most thrilling problem – anticoagulation and antiplatelet therapy during endovascular interventions – was in the focus of the session chaired by S. Abugov (Presidium members V. Vasiletz, E. Vasilieva, D. Dundua, V. Korobov, A. Mazurov, I. Pershukov, A. Perevalov, E. Sharabrin). The speakers discussed the most recent data on comparative effectiveness of platelet inhibitors Prasugrel, Ticogrelor and Clopidogrel (D. Dundua, CELT, Moscow), the comparative effectiveness and safety of direct thrombin inhibitor Bivalirudin, IIb/IIIA inhibitors and heparins (E. Vasilieva, Faculty of post-graduate education, State Medical and Stomatological University, Moscow) and the use of Russian blocker of IIb/IIIa platelet receptors during coronary angioplasty in patients with acute coronary syndrome (A. Mazurov, Russian Center of Cardiology, Moscow). The interesting discussion was ended by live transmission for the cathlab of CELT.

Another important problem – arterial embolization in different pathologies – was addressed during the next plenary session chaired by B. Momdjian. A representative presidium (G. Belozerov, G. Grishin, S. Kapranov, O. Karakulov, Yu. Shekhter, V. Ryzhkov, P. Tarazov, E. Chebotar) listened to interesting presentation on the expanding potential of organ-preserving therapy for uterine myoma using the embolization of the uterine arteries. This subject was in the focus of presentations of G. Grishin (Этой теме посвятили свои доклады Г.П. Гришин (State Medical and Stomatological University, Moscow), L. Uliatovskaya (CELT, Moscow), S. Kapranov (Russian State Medical University, Moscow). The speakers covered technical aspects of uterine arteries' embolization as well as clinical problems of this technique use for the treatment of uterine myoma. A. Spassky shared the experience of Sklifosovsky Research Institute of Emergency Care with endovascular hemostasis in patients with gastrointestinal bleeding, while R. Goloshapov-Aksenov (City Clinical Hospital, Mytischi, the Moscow region) spoke about the embolization of internal mammary artery branches in patients with early postoperative angina after the operation of mammarocoronary bypass grafting. The most interesting report reflecting the rich experience with bronchial arteries embolization in chronic obstructive lung disease complicated by bleeding was presented by M. Sitnikov (State Medical Academy, Omsk). The animated discussion was supplemented by live transmission of endovascular itnerventions from CELT and MCCIC.

The next-to-last session (moderator Z. Kavteladze, presidium members V. Buzaev, S. Drozdov, V. Lialukhin, S. Kapranov, B. Momdjan, Yu. Poliaev, A. Rudenko, V. Sokolov) was dedicated to interventional treatment of venous pathology. S. Kapranov (Russian State Medical university, Moscow) reported on the perspectives and the problems with the use of removable cava-filters. The speaker advocated the idea that all modern cava-filters should be removable. The potential of endovascular occlusion in the treatment of pelvic venous pathology in children was discussed by the authors from the Republican Pediatric Clinical Hospital (Moscow). A. Sokolov (State Medical Academy, Tver) made a detailed analysis of the possibilities of endovascular treatment of varocicele. Specialists from Bakoulev Center for Cardiovascular Surgery (Moscow) headed by N. Chigoguidze gave solid experimental validation of endovascular bypass operations (EBO) in pediatric practice.

The last session "Angioplasty of lower leg arteries" was opened and chaired by Z. Kavteladze. He introduced the presidium – S. Biriukov, I. Eroshkin, V. Ivanov, A. Maltzev, M. Malevanny, D. Ovcharenko, A. Troitzky, V. Shipovsky - and made his presentation "Angioplasty of the lower leg arteries. Endovascular treatment of critical ischemia and "diabetic foot" syndrome. Retrograde recanalization of lower leg arteries". The speaker shared his rich experience with the treatment of patients with critical ischemia and diabetic foot syndrome and presented a detailed review on this problem's state in the world. V. Ivanov reported the experience of Vishnevsky 3rd Central Military Clinical Hospital with simultaneous hybrid reconstruction

for chronic critical leg ischemia. Hybrid operations for the treatment of major lower limb arteries were in the focus of the presentation made by A. Troitzky (City Hospital №119, Khimki, the Moscow region). R. Losev (Regional Clinical Hospital, Saratov), N. Kiselev (Regional Clinical Hospital, Yekaterinburg), D. Ovcharenko (Djanelidze Research Institute of Emergency Care, St. Petersburg) and I. Eroshkin (Central Military Clinical Hospital N25, Odintzovo, the Moscow region) spoke on the role of endovascular methods in the treatment of lower limb arteries in diabetic patients.

The session ended with an interesting discussion. It was specially mentioned that more and more medical institutions in Russia deal with severe cases of critical lower limb ischemia, however the need in such care in the country is still extremely high. The promulgation of the newest methods of treatment is one of the most important tasks of Russian Scientific Society of Interventional Cardioangiology.

After a brief live transmission from the cathlab of CELT the attendees listened to the information of the President of RSSIC concerning the preparation to the 4th Congress. The Conference ended by a session of the board of RSSIC.

RECORD
of the Session of Moscow Scientific Society of Cardioangiology
December 23, 2009

Subject of the Session: «Current achievements in pharmacology and medical techniques».

Chairman: D.G. Iosseliani

In his opening remarks D.G. Iosseliani spoke of the principles of interaction between with physicians and the pharmaceutical companies and the manufacturers of expendable materials.

The following presentations have been read over:

1. E. Arkhipova, Head of cardiovascular division of LLC «Medante». «The world of Medante».
2. G. Shustova, medical counselor of «Sanofi-Aventis» company. «The news of «Sanofi-Aventis» in the field of interventional cardioangiology ».
3. T. Apukhtina, Head of the division of medical imaging tools of «Covidien» company. «New insight into contrast-induced nephropathy ».
4. «Acltelion Pharmaceuticals» company. T. Martyniuk, Head of the Department of systemic hypertension of Russian Cardiological center. «Diagnostics and treatment of pulmonary arterial hypertension ».
5. «Johnson & Johnson» company. K. Bylov, Center of Endosurgery and Lithotripsy. «Cordis' solutions in the treatment of chronic total occlusion of the lower limb arteries ».
6. I. Timashov, marketing-product manager of «Terumo» company. «The newest development by «Terumo» company.
7. L. Vedernicova, D.Med., General Director of «Raut Business» company, N. Reshetnikova, Head of the division of «CID» company. «Drug-eluting OPTIMA stent – decreasing the duration of anticoagulant therapy ».
8. Questions and discussion

Присутствовало 190 человек.

Attendance – 190 persons.

N.A. Lonskaya