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Contents

The Intermittent Percutaneous Occlusion of the Coronary Sinus in a Patient with *ST*-Elevation Acute Coronary Syndrome without Hemodynamically Significant Atherosclerotic Coronary Lesions (A Clinical Case)

B.E. Shakhov[1], E.B. Shakhov[1], D.V. Petrov[2], D.V. Volkov[2], A.S. Novikov[2], A.V. Nikolskiy[2], K.A. Kosonogov[2]*

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New ways of adequate antegrade blood flow restoration in the coronary arteries of patients with ST-elevation acute coronary syndrome (STEACS) without hemodynamically significant atherosclerotic coronary lesions have been insufficiently studied. A clinical case of a patient with STEACS without hemodynamically significant coronary lesions and slow antegrade blood flow in the left anterior descending artery (LAD) is described. The patient underwent a percutaneous intermittent occlusion of the coronary sinus for 10 minutes using the balloon catheter in the "inflation-deflation" mode. The procedure had a direct positive effect on coronary hemodynamics manifested as resolution of distal coronary spasm, improvement of myocardial perfusion and restoration of adequate antegrade flow in the LAD.

Key words: *acute coronary syndrome, ST-segment elevation, native coronary arteries, intermittent occlusion of the coronary sinus, peripheral vasospasm.*

Objectives. To demonstrate a clinical case of successful intermittent percutaneous occlusion of the coronary sinus in a patient with *ST*-elevation acute coronary syndrome (STEACS) without hemodynamically significant atherosclerotic coronary lesions.

Rationale. Up to date, new ways of antegrade blood flow restoration in the coronary arteries, management of coronary spasm, and improvement of myocardial perfusion in patients with STEACS without hemodynamically significant atherosclerotic coronary lesions have been insufficiently studied.

Methods. The patient with STEACS without hemodynamically significant atherosclerotic coronary lesions underwent the percutaneous intermittent occlusion of the coronary sinus for 10 minutes using the balloon catheter in the short-term "inflation-deflation" mode. Before and after intervention, the antegrade coronary blood flow velocity was determined and myocardial perfusion was evaluated using the TFC and QuBE methods.

Results. Coronary angiography performed in the examined patient with the clinical pattern of STEACS revealed signs of slow antegrade blood flow, coronary spasm, and reduced myocardial perfusion, mainly in the left anterior descending artery (LAD) (TFC_{LAD} = 80 frames; $d_{LAD} = 2.0 \pm 0.1$ mm; $QuBE_{LAD} = 11.2$). Intermittent occlusion of the coronary sinus had a direct positive effect on coronary hemodynamics, mainly in the LAD (TFCLAD = 55 frames; $d_{LAD} = 2.7 \pm 0.2$ mm; $QuBE_{LAD} = 26.8$). When the main cardiac vein is occluded, increasing pressure in the venules promotes the dilatation of arterioles, and, consequently, improves myocardial perfusion in the ischemic area.

Conclusions. Intermittent occlusion of the main cardiac vein has a direct effect on restoration of antegrade coronary blood flow in the LAD, relieves the signs of vasospasm and improves myocardial perfusion.

Abbreviations

STEACS – *ST*-elevation acute coronary syndrome

ECG – electrocardiography

PCI – percutaneous coronary intervention

LAD – left anterior descending artery

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CA – circumflex artery
RCA – right coronary artery

Introduction

Currently, in 30% of patients with ST-elevation acute coronary syndrome (STEACS) early invasive treatment is only limited to a diagnostic coronary angiography (1, 2). The reasons for refusal from endovascular treatment often are severe multivessel coronary lesions making an interventional cardiologist to prefer open-heart surgery and the lack of hemodynamically significant (stenoses ⩾ 50%) atherosclerotic coronary lesions. The latter is found in 10% of STEACS patients and is often associated with restoration of normal patency of the coronary arteries along with antegrade coronary "slow flow" phenomenon, distal coronary spasm, and reduction in peripheral myocardial perfusion (3).

New ways and technologies of adequate restoration of antegrade coronary blood flow, management of distal coronary spasm, and improvement of peripheral myocardial perfusion in patients with STEACS without hemodynamically significant atherosclerotic coronary lesions have been insufficiently studied up to date, and a search for them is currently a high-priority medical task.

We present a clinical case of successful application of a new method – intermittent percutaneous occlusion of the coronary sinus in a patient with STEACS in the lack of hemodynamically significant atherosclerotic coronary lesions.

Clinical case

Patient S., 34 y.o., without coronary history was admitted to the Cardiology Department of GBUZ NO City Clinical Hospital No 5 of Nizhniy Novgorod complaining of intense pressing chest pain lasting more than 60 minutes and occurred after heavy physical exercise (Table 1). The pain could not be managed with non-steroidal anti-inflammatory drugs and was accompanied by increased blood pressure up to 210/100 mm Hg.

Table 1. Characteristics of Patient S., 34 y.o.

History	Yes/No
Risk factors for coronary heart disease	
smoking	Yes
arterial hypertension	Yes
genetic predisposition	No
hyperlipidemia	No
diabetes mellitus	No
history of myocardial infarctions	No
previous coronary surgery	No
Medical therapy with	
analgesics	Yes
nitrates	No
beta blockers	No
calcium antagonists	No
aspirin	No
lipid lowering drugs	No

The clinical and electrocardiographic (ECG) pattern of STEACS was identified in the patient at the stage of initial medical contact; there were ischemic changes in anterior thoracic leads (Figure 1). Basic therapeutic treatment with opioid analgesics and antiplatelet agents, including loading dose of ticagrelor (180 mg) was started.

The patient was urgently admitted to the vascular center: the time 'initial medical contact – vascular center' was 20 minutes. On examination in the Cardiology Department: clinical stabilization, i.e., pain was relieved and blood pressure was reduced. Evidence of increasing improvement of ECG pattern was noted (Figure 2).

Electrocardiographic signs of reduction in ST segment elevation and wave T amplitude were found in leads V_1–V_3 (Table 2).

Despite the positive clinical and ECG changes, the patient was transferred to X-ray operating room equipped with angiographic complex Innova 3100-IQ (GE Medical Systems, France) to perform emergency percutaneous coronary intervention (PCI). The time from initial medical contact to PCI was 52 minutes.

Selective coronary angiography showed: right coronary blood flow. The left anterior descending artery (LAD) and its branches were without hemodynamically significant stenoses, the distal

Table 2. Comparative assessment of the main hemodynamical parameters in the patient with STEACS at the preoperative stage

Cardiac hemodynamics parameters	Initial medical contact	Vascular center	Improvement (%)
ECG pattern in thoracic leads – V_1–V_3			
ST elevation (mV)	0.28	0.08	71.5
wave *T* amplitude (mV)	0.84	0.31	63.1
Heart rate (bpm)	92	70	24.0
Systolic blood pressure (mm Hg)	210	140	33.4
Diastolic blood pressure (mm Hg)	100	80	20.0

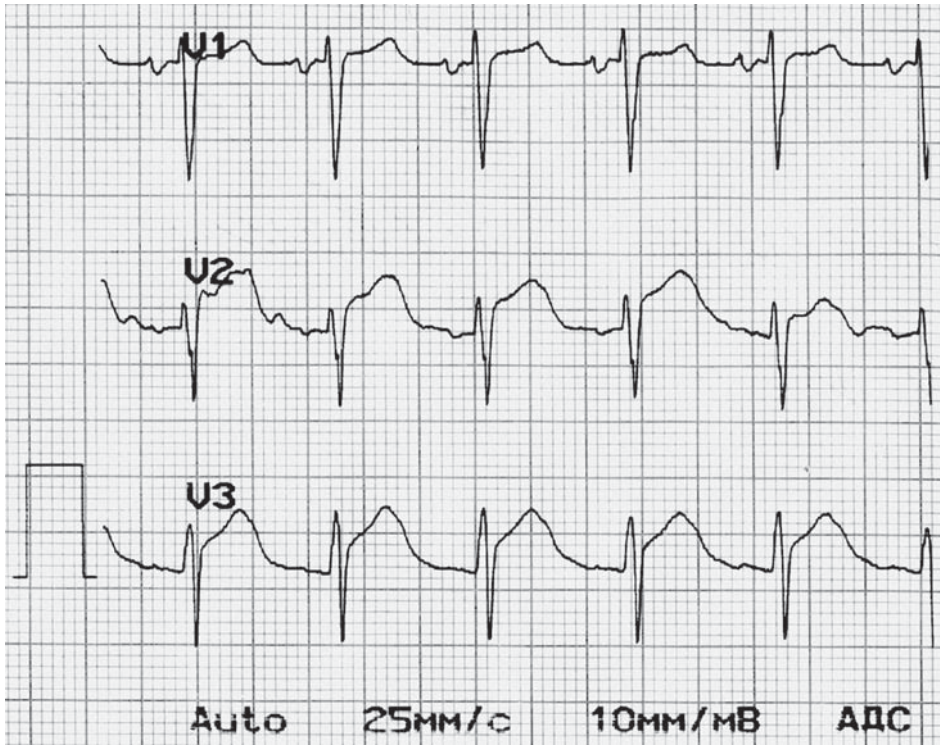

Figure 1. ECG pattern of *ST* segment elevation and wave *T* amplitude in V_1–V_3 leads.

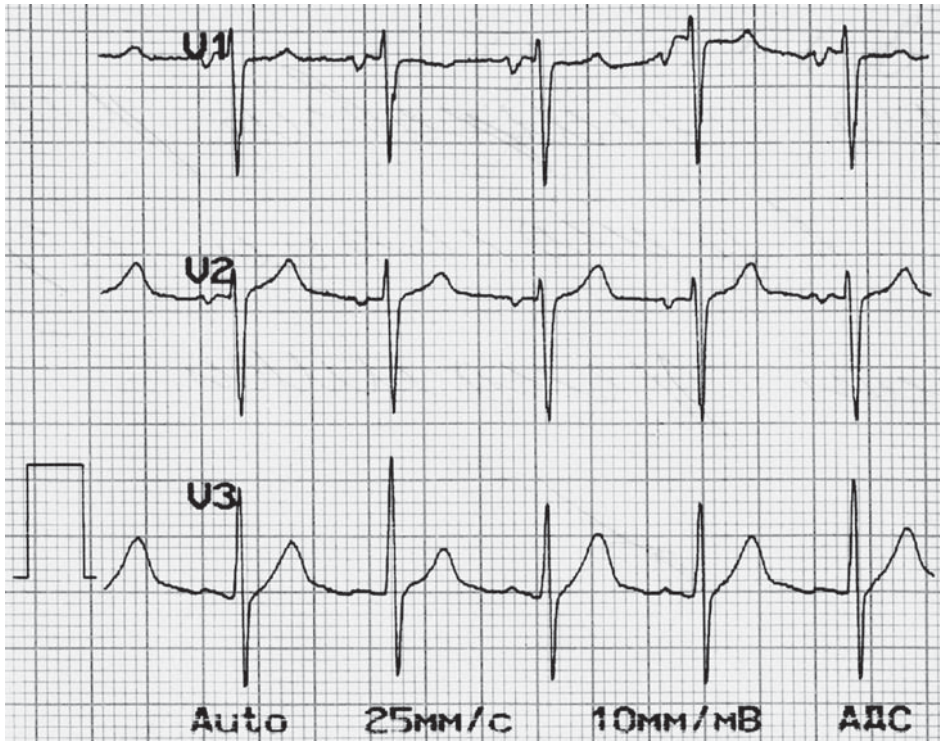

Figure 2. ECG pattern of reduction in *ST* segment elevation and wave *T* amplitude in V_1–V_3 leads.

arterial segments were narrow, with abrupt deceleration of contrast passage to the distal parts of the LAD (Figure 3).

The circumflex artery (CA) and obtuse marginal branches have no hemodynamically significant stenoses, the distal parts of the arteries are narrow. The right coronary artery (RCA) and its branches have no hemodynamically significant stenoses, there is an evidence of moderate atheromatosis in the middle part of the RCA stenosing the arterial lumen to 20%.

The antegrade blood flow velocity in the LAD, CA, and RCA and peripheral myocardial perfusion were assessed using the TFC and QuBE techniques,

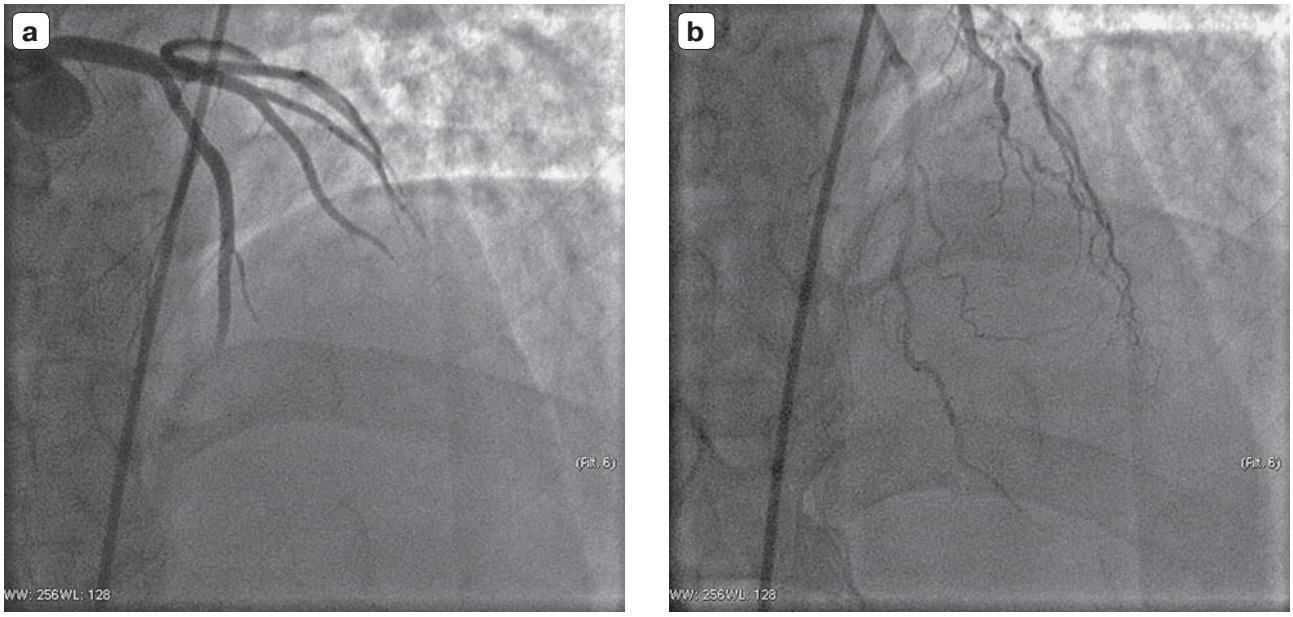

Figure 3. Angiographic signs of slowing passage of the contrast medium to the LAD: a – "pulsing" delayed opacification of the LAD; b – narrow, spastic distal parts of the LAD with the evidence of reduced peripheral myocardial perfusion.

respectively (4–6). Coronary blood flow and myocardial perfusion were analyzed at least in three angiographic projections recorded at a rate of 30 fps after intracoronary administration of nitroglycerin. The diameters of distal parts of the left and right coronary arteries were calculated using densitometric analysis of coronary stenoses (Table 3). A marked slowing of the antegrade coronary blood flow was diagnosed; the signs of distal coronary spasm in the left coronary artery branches and reduced peripheral myocardial perfusion were detected (Figure 3).

To manage the pronounced slowing of the antegrade coronary blood flow, distal coronary spasm in the left coronary artery branches, and to increase peripheral myocardial perfusion, a decision was made to perform intermittent percutaneous temporary occlusion of the coronary sinus in the patient with STEACS. Heparin 10,000 IU was intravenously administered to achieve an activated clotting time of 250–300 seconds.

To access the cardiac venous system, the right subclavian vein was punctured and a delivery system was installed in the orifice of the coronary sinus. The standard dual-lumen balloon catheter Swan-Ganz 7F was placed in proximal part of the main cardiac vein over the delivery system. The balloon catheter was thoroughly positioned near the orifice of the coronary sinus before the small cardiac vein inflow. In such a position the catheter completely stopped outflow through the main cardiac vein to the right atrium when the end balloon was maximally dilated. When the coronary sinus was temporary occluded, a free inner lumen of the balloon catheter was connected to the invasive pressure probe integral to the diagnostic complex GE Healthcare Mac-Lab/ Specials Lab 6.8 (GE Medical Systems, USA). The time spent for catheterization of the cardiac venous system and positioning of the balloon catheter was 12 minutes.

Intermittent percutaneous occlusion of the coronary sinus was performed for 10 minutes using the balloon catheter in the short-term "inflation-deflation" mode according to the method described by Van de Hoef T. P., Nolte F., Delewi R. et al., followed by obligatory control angiography 3 minutes after completion of this procedure (7). No blood outflow from the coronary sinus to the right atrium was confirmed angiographically when contrast phlebography was performed. The invasive measurement of blood pressure in the coronary sinus played an important role in determining the adequacy of temporary occlusion (Table 4).

Table 3. Calculation of the antegrade coronary blood flow velocity and assessment of peripheral myocardial perfusion in the patient with STEACS

TFS		Mean diameter (d) of the distal segment (mm)	QuBE (score)
Analyzed artery	Number of frames		
LAD	80	2.0 ± 0.1	11.2
First obtuse marginal branch	66	1.7 ± 0.2	12.3
Posterolateral branch of the RCA	42	3.1 ± 0.1	15.3

Table 4. Peculiarities of the intermittent percutaneous occlusion of the coronary sinus and criteria of its adequacy

Intermittent percutaneous occlusion of the coronary sinus	Parameter
Maximum duration of the procedure (sec)	600
Number of inflation sessions	20
Mean time of balloon inflation (sec)	19.0 ± 5.5
Number of deflation sessions	20
Mean time of balloon deflation (sec)	13.2 ± 4.3
Mean time to "plateau" of wedge pressure in the sinus (sec)	14.5 ± 4.8
Mean baseline pressure in the coronary sinus (mm Hg)	4.6 ± 1.7
Mean wedge pressure in the coronary sinus (mm Hg)	31.8 ± 6.8

During intermittent occlusion of the coronary sinus, the patient's hemodynamical parameters were stable, there was no pain. The primary hemodynamical parameters were evaluated 3 minutes after completion of the coronary sinus occlusion. Evidence of improved ECG pattern was noted (Figure 4).

Reductions in ST segment elevation and wave *T* amplitude were found in leads V_1–V_3 (Table 5).

Follow-up angiogram was performed. The antegrade blood flow velocities in the LAD, CA, and RCA were significantly increased; the distal coronary spasm in the left coronary artery branches was resolved; the distal branches of the left coronary artery were dilated and peripheral myocardial perfusion improved (Figure 5).

The signs of improved peripheral myocardial perfusion were clearly detected (Table 6).

Given the improvement of angiographic, electrocardiographic and clinical signs, the intervention was finished. Antiplatelet therapy was adjusted, calcium antagonists were prescribed.

Discussion

This clinical case demonstrates an original approach to restoration of adequate antegrade blood flow in the coronary arteries, resolution of the distal coronary spasm and improvement of the peripheral myocardial perfusion in patients with STEACS without hemodynamically significant atherosclerotic coronary lesions. Intermittent percutaneous occlusion of the main cardiac vein with induced myocardial ischemia, as an experimental approach, appeared in the middle of the 20th century, as an extension of the concept of retrograde perfusion of the coronary sinus proposed by Meerbaum S. et al. (8, 9). However, it was implemented in clinical practice in the 21st

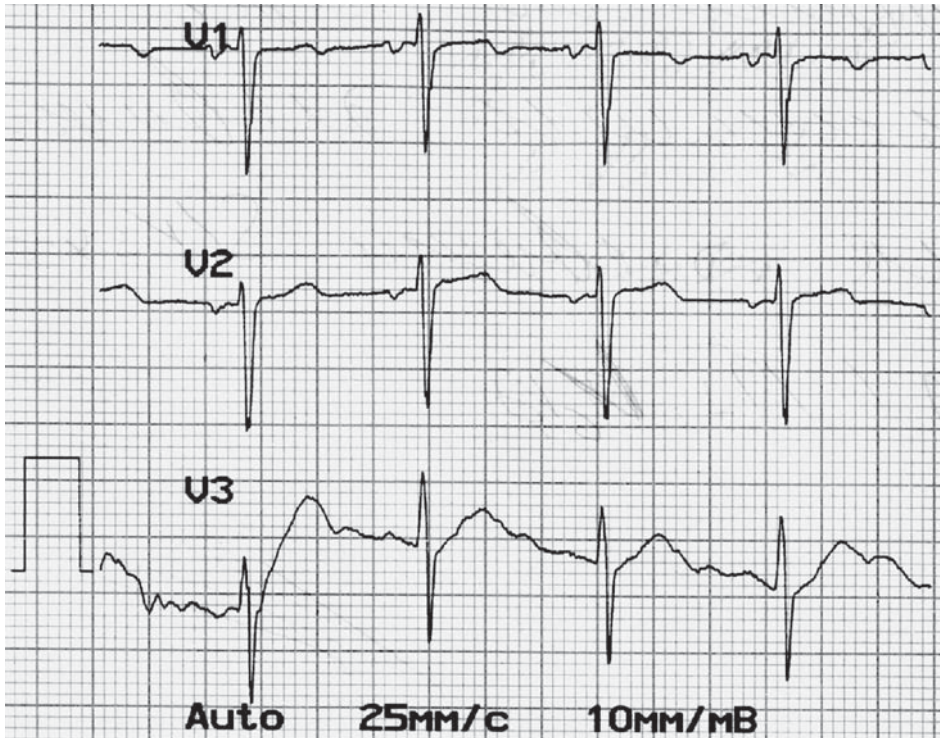

Figure 4. Improvement of ECG pattern after intermittent percutaneous occlusion of the coronary sinus (significant reduction in ST segment elevation and wave T amplitude in leads V_1–V_3).

Table 5. Comparative assessment of the main hemodynamical parameters in the patient with STEACS at the postoperative stage

Cardiac hemodynamics parameters	Initial medical contact	Vascular center	Improvement (%)
ECG pattern in thoracic leads – V_1–V_3			
ST elevation (mV)	0.08	0.04	50.0
wave *T* amplitude (mV)	0.31	0.20	35.5
Heart rate (bpm)	70	66	5.7
Systolic blood pressure (mm Hg)	140	130	7.1
Diastolic blood pressure (mm Hg)	80	75	6.3

Table 6. Calculation of the antegrade coronary blood flow velocity and assessment of peripheral myocardial perfusion in the patient with STEACS

TFS		Mean diameter (d) of the distal segment (mm)	QuBE (score)
Analyzed artery	Number of frames		
LAD	55	2.7 ± 0.2	26.8
First obtuse marginal branch	46	2.2 ± 0.2	23.4
Posterolateral branch of the RCA	37	3.3 ± 0.1	17.6

century by Van de Hoef T. P., Nolte F., Delewi R. et al. who demonstrated effective management of the peripheral myocardial perfusion via intermittent occlusion of the main cardiac vein in patients with STEACS (7, 9). Considering changes in cardiac hemodynamics demonstrated by researchers in patients with acute coronary syndrome after the intermittent occlusion of the cardiac venous system, we decided to use this technique in our patient with acute myocardial ischemia and hemodynamically insignificant coronary lesions.

So, coronary angiography revealed hemodynamically insignificant coronary lesions in our patient with the sudden onset and rapid reduction of symptomatic acute coronary syndrome with ST elevation in V1-V3 leads. The patient had the signs of slowing antegrade blood flow, distal coronary spasm, and reduced peripheral myocardial perfusion mainly in the vascular territory of the left anterior descending artery (TFC_{LAD} = 80 frames; d_{LAD} = 2.0 ± 0.1 mm; $QuBE_{LAD}$ = 11.2). According to Ong P, Athanasiadis A., Hill S. et al., such angiographic pattern may be explained by spontaneous thrombolysis in the LAD epicardial segments. In scientists' opinion, the lysis of thrombotic masses leads to microvascular embolism accompanied with peripheral coronary spasm and myocardial microcirculatory dysfunction. It should be noted that STEACS occurrence at the stage of initial medical contact in our patient

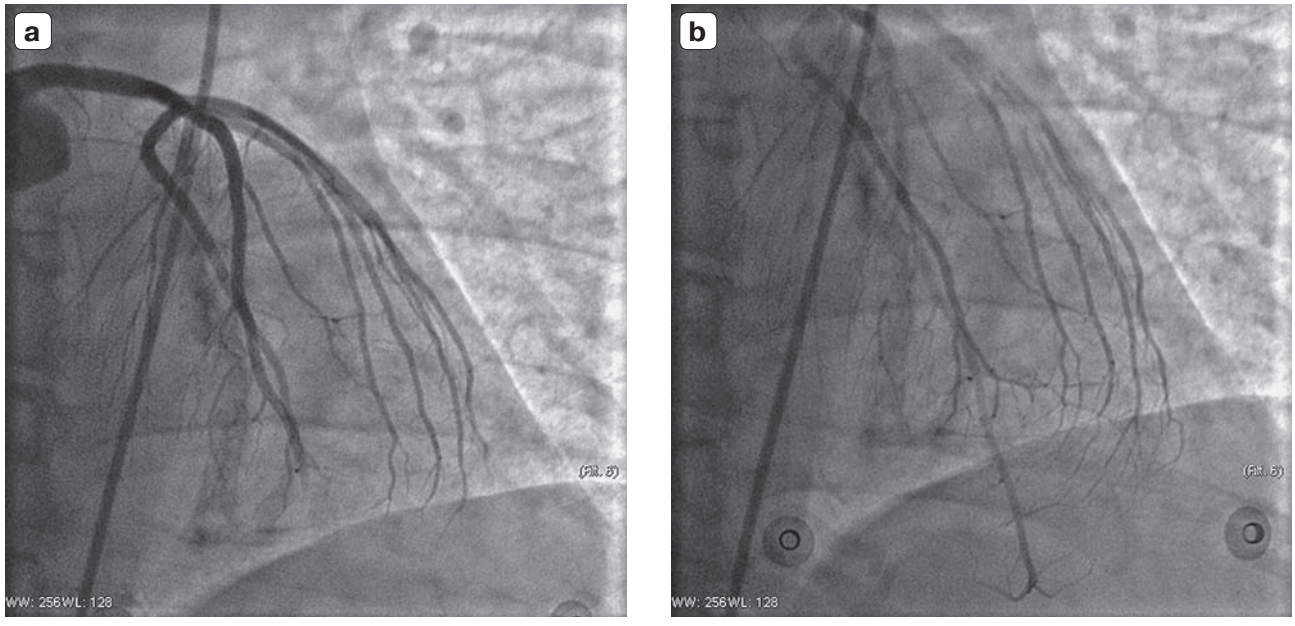

Figure 5. Angiographic signs of improved passage of the contrast medium to the LAD: a – increased velocity of contrast medium passage through the LAD; b – dilatation of the distal LAD, improvement of the myocardial perfusion.

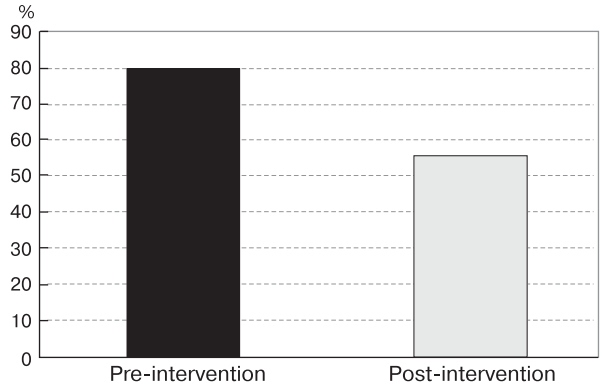

Figure 6. Accelerated antegrade blood flow in the LAD territory (assessed by TFC).

can be also explained by vasospasm-induced thrombosis of the left anterior descending artery after heavy physical exercise (3).

The intermittent percutaneous occlusion of the coronary sinus was performed according to the method developed by Van de Hoef T. P., Nolte F., Delewi R. et al. and had a direct positive effect on coronary hemodynamics, mainly in the vascular territory of the LAD (TFC@LAD = 55 frames; d@LAD = 2.7 ± 0.2 mm; QuBE@LAD = 26.8) (7). When the main cardiac vein is occluded, the venous outflow from the venules into the coronary sinus becomes difficult. Increasing pressure in the venules promotes the dilation of the arterioles and, consequently, improves peripheral perfusion of the ischemic myocardium. Intermittently increased pressure in the cardiac arteriole-venular system affects the baroreceptors of the vascular endothelium, thus indirectly inducing release of the vascular endothelial growth factor (VEGF) and activation of neoangiogenesis and angiorelaxation. A transient increase in venous pressure contributes to the dilatation of cardiac arteriole-venular microcirculation system, which in turn facilitates washout of mediators supporting inflammation, lipid peroxidation, and apoptosis (10). As a result, antegrade blood flow through the main coronary vessels is accelerated (Figure 6).

Conclusions

Intermittent percutaneous occlusion of the coronary sinus can be used in case of hemodynamically insignificant atherosclerotic coronary lesions and electrocardiographic pattern of STEACS in V_1–V_3 leads. Temporary occlusion of the main cardiac vein has a direct effect on restoration of antegrade coronary flow in the LAD, resolves the signs of vasospasm and improves peripheral myocardial perfusion as well as indirectly improves the electrocardiographic pattern after spontaneous thrombolysis.

References

1. Moiseenkov G.V., Gayfulin R.A., Barbarash O.L. et al. “Clear” coronary arteries in patients with acute coronary syndrome. Mezhdunarodnyi zhurnal interventsionnoi kardioangiologii (International Journal of Interventional Cardioangiology), 2008, 14, p. 17. (In Russian)
2. 2014 ESC/EACT Guidelines on myocardial revascularization/The Task Force on Myocardial Revascalarization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACT). Eur. Heart J. 2014, 35 (37), 2541–619.
3. Ong P., Athanasiadis A., Hill S. Vogelsberg H. et al. Coronary Artery Spasm as a Frequent Cause of Acute Coronary Syndrome: The CASPAR (Coronary Artery Spasm in Patients With Acute Coronary Syndrome) Study. J. Am. Col. Cardiol. 2008, 52 (7), 528–530.
4. Gibson C.M., Cannon C.P., Daley W.L., et al. TIMI frame count: a quantitative method of assessing coronary artery flow. Circulation. 1995, 93 (5), 879–88.
5. Porto I., Hamilton-Craig C., Brancati M., Burzotta F., et al. Angiographic assessment of microvascular perfusion--myocardial blush in clinical practice. Am. Heart J. 2010, 160 (6), 1015–1022.
6. Vogelzang M., Vlaar P.J., Svilaas T. et al. Computer-assisted myocardial blush quantification after percutaneous coronary angioplasty for acute myocardial infarction: a substudy from the TAPAS trial. Eur. Heart J. 2009, 30, 594–599.
7. Van de Hoef T.P., Nolte F., Delewi R. et al. Intracoronary Hemodynamic Effects of Pressure-Controlled Intermittent Coronary Sinus Occlusion (PICSO): Results from the First-In-Man Prepare PICSO Study. J. Intervent. Cardiol. 2012, 25 (6), 549–556.
8. Komamura K., Mishima M., Kodama K. Preliminary clinical experience with intermittent coronary sinus occlusion in combination with thrombolytic therapy in acute myocardial infarction. Jpn. Circ. J. 1989, 53, 1152–1163.
9. Mohl W., Gangl C., Jusić A., et al. PICSO: from myocardial salvage to tissue regeneration. Cardiovasc. Revasc. Med. 2015, 16, 36–46.
10. Kalinskaya A.I., Urazovskaya I.L., Vasileva E.Yu., Shpektor A.V. Spontaneous thrombolysis in patients with ST-elevation acute myocardial infarction. Creative cardiology. 2012, 1, 19–25. (In Russian)

The Results of Delayed PCI After Thrombolytic Therapy with Indirect Signs of Effectiveness in Elderly Patients with Acute Myocardial Infarction

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The retrospective study was aimed at the investigation of the results of delayed PCI after thrombolytic therapy with indirect signs of effectiveness in elderly patients (≥75 years) with acute myocardial infarction. The authors conclude, that the delayed PCI appropriately performed in patients ≥75 y.o. with acute myocardial infarction who underwent thrombolytic therapy and had indirect ECG signs of coronary reperfusion is relatively safe intervention but its benefit requires additional confirmation.

Key words: *myocardial infarction, myocardial reperfusion, thrombolysis, PCI, pharmacoinvasive reperfusion, elderly.*

Aim. The aim of this study was to investigate the efficacy and safety of percutaneous coronary interventionafter thrombolytic reperfusion withindirect reperfusion signs in elderly patients with acute myocardial infarction.

Material and methods. Patients aged ⩾75 years with acute myocardial infarction and successful thrombolysis were included in this study. The criterion of exclusion was death in the first day of admission to hospital. A total of 96 patient charts were used for the analysis.

Results. In these patients, 31% of patients were selected for delayed PCI. In comparison, patients, not selected for PCI, were older, more often were women, more often had stroke in anamnesis, and less often presented with cardiogenic shock. Coronary angiography in patients with electrocardiographic signs of reperfusion demonstrated the presence of occlusion of infarct-related artery in 56.7% of cases. The stent implantation was performed in 70% of cases. The reasons for non-performance of stent implantation were severe coronary disease with calcinosis (67%) and the stenosis ⩽70% which did not require angioplasty (37%). The rates of recurrent myocardial infarction (ReMI) and lethality in patients aged ⩾75 years with acute myocardial infarction (MI) as well as electrocardiographic signs of reperfusion after thrombolysis did not differ between groups of conservative therapy and delayed PCI: ReMI was 9.1% vs 6.7% and lethality – 13.6% and 10.0% accordingly.

Conclusion. The routine delayed PCI performing in elderly patient with acute myocardial infarction after successful thrombolysis is safe but its benefit remains still unclear.

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Abbreviations:

CA – coronary artery
CAG – coronary angiography
AMI – acute myocardial infarction
CVA – cerebrovascular accident
TLT – thrombolytic therapy
PCI – percutaneous coronary intervention
LVEF – left ventricular ejection fraction

Introduction

According to the current clinical guidelines, all patients with ST-elevation acute myocardial infarction (AMI) after successful thrombolytic therapy (TLT) should undergo coronary angiography (CAG) and, if indicated, percutaneous coronary intervention (PCI) (1). However, the guidelines are based on studies that usually include a very small proportion older patients compared to general population (2, 3, 4). As a consequence, the mortality rate in observational studies (registries) is significantly higher than in randomized studies.

Therefore, the guidelines for routine PCI after successful thrombolysis in elderly patients are less convincing than for younger patients.

On one hand, according to the published results, full compliance with the guidelines for pharmacoinvasive reperfusion improves prognosis even in patients ⩾85 y.o., (5). However, conflicting data also exist. In optional analysis from TRANSFER-AMI trial of pharmacoinvasive revascularization, patients were divided by risk of mortality according to GRACE scale at the time of admission (6). The low/moderate and high risk groups included patients with a risk of <5% and ⩾5%, respectively. It was found that pharmacoinvasive reperfusion reduced the incidence of the composite endpoint in the low/moderate risk group: 2.9% versus 8.1% ($p < 0.001$), but PCI routinely performed after thrombolysis in the high risk group worsened outcomes: 27.8% versus 13.8% ($p = 0.025$) and this difference maintained for 1 year. Age is one of the main criteria in the GRACE scale. Mean age in the low/moderate and high risk groups was 55 and 75 y.o., respectively. Based on these results, post-thrombolytic routine PCI may be unjustified in older patients, especially those with signs of reperfusion in the infarct-related coronary artery (CA).

Aim. Analysis of the effectiveness and safety of delayed PCI in patients ⩾75 y.o. with AMI after successful thrombolysis.

Material and methods

Case histories of the Emergency Cardiology Department of the Research Institute for Cardiology (Tomsk) for 2010–2014 were retrospectively analyzed. The study included patients ⩾75 y.o with AMI who underwent TLT and had indirect signs of coronary reperfusion on ECG (reduction of ST elevation by ⩾50% in the informative leads). The exclusion criterion was death within the first 24 hours. 96 case histories were selected according to these criteria. The clinical and historical characteristics of patients on admission, CAG results, PCI effectiveness, incidence of complications and outcomes were analyzed. This analysis compared patients who continued conservative therapy and who underwent routine delayed PCI.

The results were statistically processed using STATISTICA 8.0 for Windows. Distribution was checked for normality using Kolmogorov–Smirnov test with Lilliefors correction. Quantitative variables were presented as Me (25–75%Q), where Me is median and (25–75%Q) – interquartile range. Intergroup differences were assessed using Mann–Whitney U-test. Comparative analysis of categorical independent variables was performed using χ^2 test or Fisher's exact test for 2×2 tables for expected value of < 5 in the table cell. The critical significance p-level in all procedures of statistical analysis was 0.05.

Results

Among 96 AMI patients ⩾75 years after successful TLT, only 30 patients (31%) were referred for delayed PCI within 24 hours after TLT as a part of pharmacoinvasive reperfusion strategy. The remaining patients continued conservative therapy. The main clinical and historical characteristics of the patients from Group 1 (conservative therapy) and Group 2 (delayed PCI) on admission and parameters of thrombolytic therapy are shown in Table 1. The patients who were not referred for PCI after successful TLT were older: 81 y.o. versus 77 y.o. ($p < 0.01$), more often were women: 71.2% versus 46.7% ($p < 0.05$), more often had a history of stroke: 18.2% versus 3.3% ($p < 0.05$), and less frequently were diagnosed with cardiogenic shock: 3% versus 10% ($p < 0.05$), streptokinase was the most common thrombolytic agent: 78.8% versus 53.3% ($p < 0.01$).

The treatment results are presented in Table 2. Despite the fact that all patients had indirect evidence of myocardial reperfusion after TLT, diagnostic CAG in 5 patients from Group 2 (16.7%) revealed total CA occlusion (TIMI-0) and in 12 patients (40%) the blood flow was consistent with TIMI-1. Thus, there was no blood flow in the infarct-related CA in 56.7% of cases. The blood flow was TIMI-2 and TIMI-3 in 8 (26.6%) and 5 (16.7%) patients, respectively. Among all these patients, angioplasty and CA stenting were performed and blood flow TIMI-3 was achieved only in 70% of cases (21 patients). In other cases, interventions were limited to diagnostic CAG. The reasons for non-performance of PCI were as follows: complex coronary anatomy with calcification – 6 patients (66.7%), residual stenoses of <70% requiring no angioplasty – 3 patients (33.3%).

Medical therapy did not differ between the groups. The incidence of recurrent AMIs did not significantly differ: 6 patients (9.1%) and 2 patients (6.7%) in Group 1 and Group 2, respectively. In 2 patients from Group 1 the disease was complicated by ischemic stroke. No hemorrhagic strokes were observed. Only

Table 1. Clinical and historical characteristics of patients

	Successful TLT 66 pts	Successful TLT followed by PCI, 30 pts	p
Age, Me (Q1-Q3)	81 (78–84)	77 (75–82)	<0.01
Sex: F	47 (71.2%)	14 (46.7%)	<0.05
M	19 (28.8%)	16 (53.3%)	
Localization of MI:			ns
Anterior	26 (39.4%)	12 (40%)	
Posterior	37 (56.1%)	15 (50%)	
Circular	3 (4.5%)	3 (10%)	
PICS	19 (28.8%)	7 (23.3%)	ns
DM	22 (33.3%)	8 (26.7%)	ns
Smoking	10 (15.2%)	9 (30%)	ns
Obesity	21 (31.8%)	7 (23.3%)	ns
AH	62 (93.9%)	27 (90%)	ns
Dyslipidemia	51 (77.3%)	28(93.3%)	ns
Renal failure	23 (34.8%)	8 (26.7%)	ns
Cancer	5 (7.6%)	3 (10%)	ns
History of CVA	12 (18.2%)	1 (3.3%)	<0.05
Killip			
1	39 (59.1%)	10 (33.3%)	<0.05
2	18 (27.3%)	14 (46.7%)	
3	7 (10.6%)	3 (10%)	
4	2 (3%)	3 (10%)	
TLT administration:			ns
pre-hospital stage	25 (37.9%)	17 (56.7%)	
in-hospital stage	41 (62.1%)	13 (43.3%)	
Drug:			
streptokinase	52 (78,8%)	16 (53,3%)	<0,01
alteplase	2 (3%)	1 (3,3%)	
tenecteplase	3 (4,6%)	10 (33,3%)	
prourokinase	9 (13,6%)	3 (10,1%)	
Time “MI-TLT”, min	177.5 (115–340)	207.5 (130–330)	ns

moderate and massive bleedings according to the TIMI criteria were analyzed for statistical processing. No massive bleedings were observed in both groups . The incidences of moderate bleedings did not significantly differ: 13 (19.7%) versus 10 (33.3%) in Group 1 and Group 2, respectively. Contrast-induced nephropathy after CAG/PCI was observed in 2 patients (6.7%). In-hospital mortality between the groups did not differ: 9 patients (13.6%) versus 3 patients (10%) in Group 1 and Group 2, respectively.

Discussion

According to the data from this study, referral for delayed PCI after successful thrombolysis depends on age among elderly patients: the older the patient, the rarer the procedure. This fact corresponds to the literature data, in which age is considered as one of the reasons to abstain from invasive procedure (7, 8). This pattern persists in patients ⩾75 y.o. as well. With older age, PCI is limited by increased number of co-morbidities and more severe coronary lesions. In this study, one of the reasons to abstain from PCI was a history of cerebral vascular accident (CVA): its incidence was higher in the non-PCI group compared to PCI group. Firstly, it is a sign of multifocal atherosclerosis suggesting more severe coronary lesions and reducing the chance to perform PCI after diagnostic CAG. Secondly, the baseline patient’s functional status is considered when deciding on PCI. If his/her status prior to AMI was severe (patient with a history of CVA was restricted in his/her movements, poorly took care of himself/herself), it is usually an additional reason to abstain from PCI.

On the contrary, the cardiogenic shock is an indication for PCI, and the results of this study confirm the implementation of this clinical guideline: PCI group included significantly more patients with cardiogenic shock.

Although streptokinase as a thrombolytic agent was used in more than a half of the cases in both groups, in older patients (Group 1)

Table 2. Treatment and results

	Successful TLT without PCI 66 pts	Successful TLT followed by PCI, 30 pts	p
Pre-PCI CA blood flow (by TIMI)			
0		5 (16.7%)	
1		12 (40%)	
2		8 (26.6%)	
3		5 (16.7%)	
PCI/only CAG		21 (70%)/9 (30%)	
Number of stents:			
0 (only CAG)		9 (30%)	
1		19 (63.3%)	
2		2 (6.7%)	
Post-PCI CA blood flow (by TIMI):			
0		1 (3.3%)	
1		1 (3.3%)	
2		7 (23.4%)	
3		21 (70%)	
Type of stent:			
bare metal stent		17 (81%)	
drug-eluting stent		4 (19%)	
Reason for non-performance of PCI:			
complex CA anatomy		6 (66.7%)	
stenosis <70%		3 (33.3%)	
ACE inhibitors	55 (83.3%)	27 (90%)	ns
β-adrenoblockers	62 (93.9%)	26 (86.7%)	ns
Diuretics	36 (54.5%)	21 (70%)	ns
Antiaggregants	66 (100%)	30 (100%)	ns
Anticoagulants	66 (100%)	30 (100%)	ns
Bleedings (moderate by TIMI)	13 (19.7%)	10 (33.3%)	ns
Contrast-induced nephropathy		2 (6.7%)	
No-reflow phenomenon		2 (6.7%)	
LV ejection fraction (%)	51 (45-58)	53 (45-60)	ns
Recurrent MI	6 (9.1%)	2 (6.7%)	ns
CVA	2 (3%)	0 (%)	ns
Death	9 (13.6%)	3 (10%)	ns

it was used more frequently than in "younger" patients (Group 2). As early as in 1993, GUSTO-1 study comparing streptokinase and alteplase demonstrated less frequent hemorrhagic strokes with streptokinase: 0.54% versus 0.72%. Increased risk of intracranial bleedings related to tissue plasminogen activators compared to streptokinase was confirmed by subsequent meta-analyses and registers (9). A history of CVA is associated with an increased risk for hemorrhagic stroke. Therefore, for safety reasons it seems quite natural to use streptokinase in older patients with a history of CVA. Currently, alteplase and tenecteplase are used more and more frequently, therefore streptokinase has become less important but retains its place in the guidelines (1); there is no reason to completely abandon this drug, especially given its advantage in terms of safety in patients with an increased risk for hemorrhagic stroke.

Although all patients after thrombolysis had indirect ECG signs of CA reperfusion, delayed CAG in patients from Group 2 revealed no coronary blood flow in the infarct-related CA in 56.7% of cases. Therefore, currently used indirect signs of coronary reperfusion (reduction of ST elevation by ⩾50%) usually don't reflect epicardial blood flow restoration in elderly patients. It can be assumed that decrease in *ST* elevation in this case reflects only improvement of myocardial tissue perfusion, possibly as a result of improved collateral blood flow.

To assess the degree of myocardial perfusion ("blush"), TIMI myocardial perfusion grade (TMP grade) is used (10). This parameter is known to be an independent predictor of outcome. And the lowest mortality was observed in patients with proper TIMI 3 blood flow in the epicardial artery in combination with restored TMP grade 3 (11). Therefore, improved myo-

cardial perfusion does not imply refusal to restore antegrade blood flow in the epicardial coronary artery. According to the results of this study, the indirect ECG signs of coronary reperfusion in most cases do not reflect restoration of antegrade blood flow in the infarct-related CA in elderly patients; therefore, it is logical to conclude that all these patients, despite positive ECG changes, require not delayed but rescue PCI. But this approach has not been studied and its efficacy and safety are still unclear.

In most patients referred for an invasive procedure (70% of cases), PCI with stenting could be performed. The rate of PCI-related complication seems to be quite low. Insignificant increase in the number of bleedings in the PCI group was caused by bleedings from the femoral artery puncture site. Currently, this problem is solved by more frequent use of radial access and use of devices "suturing" the femoral artery puncture site. Post-PCI contrast-induced nephropathy was observed only in 2 patients (6.7%). Additionally, no-reflow phenomenon was noted in 2 patients (6.7%) after mechanical recanalization of occluded CA. Therefore, delayed PCI performed as recommended in the analyzed patients appears to be relatively safe, but its benefit requires additional confirmation. With more patients, the number of recurrent AMIs after PCI can statistically significantly decrease. The same result is possible in case of long-term follow-up.

When analyzing the results of this study, it should be considered that patients who died within 24 hours were not included in the analysis. Among these patients, many subjects are admitted very late, with a long delay from the disease onset, with contraindications for antithrombotic therapy, and often with signs of refractory cardiogenic shock. All therapeutic measures, including reperfusion, are ineffective in these patients. According to the guidelines, these patients require primary PCI; therefore, to examine TLT efficacy in them is unreasonable. To obtain more homogeneous material suitable for statistical processing, it was decided to exclude them from the study. Therefore, it is necessary to consider that the most severe patients remained beyond the scope of this analysis, and, consequently, conclusions.

It also should be noted that the left ventricle ejection fraction was preserved in the examined patients from both groups: on average >50%. Given that the analysis did not include the patients who died within the first 24 hours after admission, it can be assumed that the patients with very low ejection fraction died within these 24 hours. Therefore, the obtained results and conclusions are valid for patients with preserved LVEF, which can be defined, given the dispersion of values, probably as ⩾45%.

Conclusions

Among patients ⩾75 y.o. with acute myocardial infarction after successful thrombolytic therapy, only 31% are referred to delayed PCI as part of pharmacoinvasive myocardial reperfusion.

In patients ⩾75 y.o., older age, previous CVA and lack of cardiogenic shock are associated with less frequent referral for delayed PCI after successful thrombolytic therapy.

In patients ⩾75 y.o. with indirect signs of myocardial reperfusion after thrombolytic therapy, there was no blood flow in the infarct-related coronary artery in 56.7% of cases (TIMI 0-1).

Coronary angiography and delayed percutaneous intervention (CA stenting) in patients ⩾75 y.o. with acute myocardial infarction after thrombolytic therapy with indirect signs of coronary reperfusion are performed as a part of pharmacoinvasive reperfusion in 70% of cases. In other cases, PCI cannot be performed most commonly due to severe coronary disease.

There were no differences in the incidences of recurrent myocardial infarction and mortality in patients ⩾75 y.o. with indirect signs of myocardial reperfusion after successful thrombolytic therapy between the continued conservative therapy group and delayed PCI group. Therefore, the appropriateness to refer elderly patients for routine PCI after successful thrombolysis requires additional confirmation.

References

1. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur. Heart J. 2012, 33, 2569–2619.
2. Konrat C., Boutron I., Trinquart L. et al. Underrepresentation of Elderly People in Randomised Controlled Trials. The Example of Trials of 4 Widely Prescribed Drugs. PLoS ONE 2012, 7(3), e33559. doi:10.1371/journal.pone.0033559.
3. Le Quintrec J., Bussy C., Golmard J.-L. et al. Randomized Controlled Drug Trials on Very Elderly Subjects: Descriptive and Methodological Analysis of Trials Published Between 1990 and 2002 and Comparison With Trials on Adults. J. Gerontol. 2005, 60 (3), 340–344.
4. Alexander K.P., Newby L.K., Armstrong P.W. et al. Acute coronary care in the elderly, part II: ST-segment-elevation myocardial infarction: a scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology: in collaboration with the Society of Geriatric Cardiology. Circulation. 2007, 15 (19), 2570–2589.

5. TjiaJ., Allison J., Saczynski J.S. et al. Encouraging trends in acute myocardial infarction survival in the oldest old. Am. J. Med. 2013, 126 (9), 798–804.
6. Yan A.T., Yan R.T., Cantor W.J. et al. for the TRANSFER-AMI Investigators. Relationship between risk stratification at admission and treatment effects of early invasive management following fibrinolysis: insights from the Trial of Routine Angioplasty and Stenting After Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction (TRANSFER-AMI). Eur. Heart J. 2011, 32 (16), 1994–2002.
7. Ehrlich A.D., Kharchenko M.S., Barbarash O.L. et al. Compliance with the guidelines for treatment of acute coronary syndrome in clinical practice of Russian hospitals and in-hospital outcomes (RECORD-2 registry data). Kardiologya (Cardiology). 2013, 1, 14–22. (In Russian)
8. Vyshlov E.V., Filyushkina V.Yu., Krylov A.L., Markov V.A. Effectiveness of reperfusion procedures in patients ⩾70 y.o. with ST-elevation myocardial infarction. Sibirskij Meditsinkij Zhurnal (Siberian Medical Journal) (Tomsk). 2014, 1 (29), 25–30. (In Russian)
9. Huynh T., Cox J.L., Massel D. et al. Predictors of intracranial hemorrhage with fibrinolytic therapy in unselected community patients: a report from the FASTRAK II project. Am. Heart J. 2004, 148 (1), 86–91.
10. Rind E., ArbelY., Finkelstein A. et al. Angiographic Evaluation of Epicardial and Microvascular Coronary Flow. Israel. Med. Assoc. J. 2009, 11, 173–177.
11. Gibson C.M., Cannon C.P., Murphy S.A. et al. Relationship of the TIMI myocardial perfusion grades, flow grades, frame count, and percutaneous coronary intervention to long-term outcomes after thrombolytic administration in acute myocardial infarction. Circulation. 2002, 23, 105 (16), 1909–1913.

Hybrid Myocardial Revascularization in Multivessel Coronary Disease. State-of-the-Art

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This article deals with the issue of hybrid coronary surgery, its role in surgical treatment of patients with multivessel coronary disease and stable CHD. The literature data comparing hybrid myocardial revascularization with coronary artery bypass grafting and percutaneous coronary intervention are presented.

Key words: *hybrid myocardial revascularization, percutaneous coronary intervention, coronary artery bypass grafting.*

List of abbreviations:

CHD – coronary heart disease
AC – artificial circulation
MI – myocardial infarction
CABG – coronary artery bypass grafting
CA – circumflex artery
CVA – cerebrovascular accident
RCA — right coronary artery
LAD – left anterior descending artery
PCI – percutaneous coronary intervention
BMS – bare metal stent
DES – drug-eluting stent
MID CAB – minimally invasive direct coronary artery bypass
OPCAB – off-pump coronary artery bypass

Today, coronary artery bypass grafting and percutaneous coronary intervention are the most common options of myocardial revascularization. To combine the benefits of both treatment options and eliminate their disadvantages, a hybrid method of myocardial revascularization including mammary bypass grafting to the left anterior descending artery and percutaneous coronary intervention for other coronary vessels was proposed. The hybrid revascularization may be performed either simultaneously in a hybrid operating room, or in two steps. The first step may include either percutaneous coronary intervention or left internal thoracic artery bypass grafting. The sequence of the steps in the hybrid approach is still disputable; each option has its advantages and disadvantages. Currently, there are no clear recommendations on hybrid revascularization in patients eligible for coronary bypass grafting and percutaneous coronary intervention. European guidelines on myocardial revascularization – 2014 demonstrate the lack of consensus on the place of hybrid revascularization; in these guidelines the indications for hybrid procedures are IIB class, the level of evidence is C (experts' opinion). Only prospective randomized studies will determine the place of the hybrid method among other options of myocardial revascularization. One study "Hybrid REvascularization Versus Standards (HREVS)" (http://www.clinicaltrials.gov/ct2/show/NCT01699048) comparing three methods of myocardial revascularization was initiated at our site.

Coronary heart disease (CHD) remains the leading cause of disability and mortality of working populations worldwide. In Russia, more than half of all deaths are caused by the cardiovascular diseases. Among cardiovascular diseases, the main is coronary heart disease accounting for more than half of deaths from cardiovascular diseases.

Myocardial revascularization improves quality of life and long-term results in CHD patients which is confirmed by numerous studies and is the reason for its wide distribution (1). Today coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) are the most common options of myocardial revascularization.

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The issue of choosing the optimal strategy of revascularization remains controversial and depends on many factors, such as morphology and localization of coronary lesions, co-morbidities and possible use of dual antiplatelet therapy (2, 3). CABG, since its introduction in practice by R. Favaloro and D. Effler in 1967, has become one of the most important surgeries in the history of medicine. Although CABG is an established approach in myocardial revascularization, rapidly developing PCI and medical therapy are prerequisites for alternative minimally invasive options.

The main advantage of CABG over PCI is the left internal thoracic artery grafting to the left anterior descending artery (LAD), which is an independent predictor of survival and lack of need for repeated revascularization in the long-term period (4, 5). Additionally, the long-term patency of arterial grafts is apparently higher compared to venous ones. The lifespan of mammary graft makes it optimal conduit for LAD revascularization. According to some authors, 5-year patency of the internal thoracic artery is 96% and slightly reduces to 93% by Year 15 (6). However, bypass technique plays an important role in the mammary graft functioning. For example, Hayward et al. demonstrated 96% 5-year patency of the grafts in situ, while mammary grafting with free conduit decreased the patency to 89% (7).

The main CABG disadvantages are invasiveness and high probability of perioperative complications (post-CABG MI 10%, post-CABG stroke 1.4–3.8%, infectious complications 2–6%, mediastinitis 0.45–5%) (8–11). Off-pump beating CABG does not solve the problem of perioperative complications. A certain positive shift occurred when Benetti suggested the left-sided minithoracotomy for LAD bypass grafting using the internal thoracic artery (12), this technique is called MID CAB (minimally invasive direct coronary artery bypass). The procedure widely used by Calafiore (13) could be considered a natural development of the "beating heart" technique, because it emphasized the potential of minimal access for coronary bypass surgery. However, the minimal accesses are of limited use in multivessel coronary lesions (14–17).

Another CABG-related disadvantage is a high likelihood of failure of the venous grafts in the long-term period, but currently they are most commonly used. The probability of dysfunction of the venous grafts ranges from 13% to 29% during Year 1 and up to 50% in 10 years, respectively (18). Besides disadvantages, CABG has a number of limitations that increase surgery-related risks: advanced age, reduced ejection fraction, history of stroke, diffuse atherosclerosis and aortic calcification, concomitant pulmonary pathology, and renal dysfunction (19).

The main advantages of PCI over CABG are lower invasiveness, rapid recovery and lower incidence of perioperative complications (in-hospital mortality 1.27%, PCI-related MI 15%, PCI-related CVA 0.22%, access site complications 2–6%) (20). Currently, there is a growing number of evidence suggesting satisfactory long-term results of PCI using bare metal stents (BMS), especially drug-eluting stents (DES) (21, 22). It has been well established that DES reduce significantly the incidence of in-stent restenosis and, consequently, the rate of repeated revascularization. A meta-analysis of 38 randomized studies comparing the immediate and long-term (up to 4 years) results of DES (sirolimus and paclitaxel) and BMS implantations was performed. The total number of patients was 18,023. The groups did not significantly differ in the rates of death and myocardial infarction, while the rates of repeated revascularization were 20%, 7.1%, and 5.1% in the BMS group, paclitaxel-eluting stents group, and sirolimus-eluting stents group, respectively ($p < 0.001$ versus BMS) (22).

Although the comparative data on venous grafts versus stents are limited, the PCI results in respect of repeated revascularization in both target lesions and non-LAD target vessels are similar to venous grafts or radial arterial grafts (23, 24).

A meta-analysis of 10 randomized trials comparing the long-term results of CABG and PCI in 7,000 patients showed no difference in the rates of death and myocardial infarction (MI) in the long-term period of 8 years (25). However, several studies demonstrated the superiority of CABG over medical therapy and PCI in multivessel coronary lesions. According to the Syntax study, the analysis of the primary endpoints including MACCE (death, MI, stroke, repeated revascularization) in patients with multivessel disease demonstrate significant differences between the PCI and CABG groups if Syntax Score is >22 (26).

To combine the benefits of both treatment options and eliminate their disadvantages, a hybrid method of myocardial revascularization including mammary bypass grafting to the LAD and PCI of non-LAD vessels was proposed.

Holzhey defined the hybrid technique of blood flow restoration in the multivessel coronary lesions as LAD grafting using mammary coronary bypass graft in situ and combined PCI of other coronary vessels within 3 days (27). In 1996, Angelini et al. published the first experience of hybrid coronary revascularization (28). The concept of hybrid revascularization is based on the successful results of the LAD grafting using the left internal thoracic artery via minimally invasive technique without sternotomy or manipulation of the aorta (MID CAB), which reduces the risk of neurological, infectious and hemorrhagic complications, as well as on satisfactory results of DES functioning compared with autovenous grafts (29–31).

Several studies demonstrated the safety of MID CAB. For example, McGinn et al. published their own experience of MID CAB in 450 patients. The mortality was 1.3%; the conversion to sternotomy was reported in 3.8% of cases (32). Another study of MID CAB and CABG complications demonstrated no significant differences in the number of MACCE (death, myocardial infarction, stroke, repeated revascularization); however, the total number of complications was significantly higher in the CABG group (37% versus 12%, respectively) (33). When comparing the number of strokes by surgery type, the superiority of MID CAB over CABG was noted (1.6% versus 3.8%, respectively) (34). Harry Lapierre et al. provided an interesting comparison of two cardiosurgical techniques: MID CAB (n = 150) and OPCAB (n = 150) performed by one surgeon. In both groups, repeat surgeries were performed for bleeding and graft revision in 4 (2.7%) and 1 (0.7%) cases each. In the MID CAB group, conversion to sternotomy occurred in 10 (6.7%) patients. No deaths or perioperative MIs were observed in both groups. Wound infection developed in 0 and 6 (4.0%) patients in the MID CAB group and OPCAB group, respectively ($p = 0.002$). Mean in-hospital stay duration was 5.4 days and 7.2 days in the MID CAB group and OPCAB group, respectively ($p = 0.02$). Mean time to restore completely the physical activity (the ability to walk 30 minutes or more per day and no restrictions when the upper body is used for daily activities) was 12 days in the MID CAB group and more than 5 weeks in the OPCAB group (35).

The cohort of patients eligible for hybrid myocardial revascularization includes patients with coronary heart disease and multivessel coronary lesions involving the proximal part of the left anterior descending artery along with stenoses of other non-LAD vessels suitable for PCI. Patients with chronic occlusions, calcified and prolonged lesions are more suitable for conventional CABG. Patients who have unsuitable conduits, previous sternotomy, diseases of the ascending aorta, can also be eligible for hybrid surgery. The hybrid approach is especially promising in the high-risk population due to the lesser surgical trauma (36, 37).

The hybrid revascularization may be performed either simultaneously in a hybrid operating room, or in two steps. The first step may include either PCI or MCBG. The sequence of the steps in the hybrid approach is still disputable; each option has its advantages and disadvantages. The advantages of PCI if it is performed at the first step are as follows: possible simultaneousl coronary angiography and PCI; loading dose of antiplatelet agents is administered before the procedure; possible hybrid revascularization after stenting of the symptom-related lesion in acute coronary syndrome; any negative PCI results may be adjusted further with open heart surgery. The disadvantages are as follows: surgical step is performed while on the dual antiplatelet therapy, thus increasing the risk of bleeding; and inability to evaluate the patency of the mammary graft to the LAD (38, 39).

Zhao et al. reported 112 hybrid procedures, with PCI at the first step in 96% of cases. The results of hybrid approach were compared to the CABG results (n = 254). Bleeding-related repeat interventions were performed in 3% of cases in each group. There were no significant differences in the number of blood transfusions and volume of drained fluid. The long-term expected survival was higher in the CABG group, especially when SyntaxScore was >33 (40).

However, the initial revascularization of the LAD via minimal access has several advantages, i.e.: angiographical monitoring of the mammary graft; lesser risk of bleeding during surgical intervention since dual antiplatelet therapy is prescribed later, before the second step; revascularization of a large LAD territory reduces the risk of further PCI. The disadvantages are potential acute coronary events in the non-revascularized CA and RCA at the first step and, subsequently, potential unsuccessful PCI in case of complex stenting techniques; after unsuccessful PCI, repeat direct revascularization via median sternotomy should be considered.

The problem of in-stent thromboses and bleedings related to the antiplatelet and anti-

coagulant supportive therapy remains unresolved in the hybrid surgery. No guidelines for antiplatelet therapy in hybrid revascularization exist. Some investigators reported their experiences in the use of antiplatelet therapy with varying degree of success to prevent acute in-stent thrombosis and perioperative bleeding. The problem is partly related to the step-by-step approach and timing of treatment. If MCBG and PCI are performed simultaneously, a loading dose of clopidogrel (300 or 600 mg) is given either immediately prior to surgery (15), or after MCBG (41, 42), or when PCI is completed (15, 43, 44). Interestingly, the maximum antiplatelet effect is achieved only a few hours after a loading dose (45), hence there is a time period of incomplete hypoaggregation during the procedure, which may cause in-stent thrombosis. The risk of acute in-stent thrombosis varies from 0% to 7%. According to available data on hemorrhagic complications, the hybrid revascularization is not associated with an increased risk of bleeding. Some studies demonstrate a lower risk of bleedings compared to conventional CABG (15, 41, 44). New P2Y12 inhibitors, such as prasugrel and ticagrelor, have a more pronounced hypoaggregation effect with a faster onset and shorter half-life compared to clopidogrel (45). Due to these properties, the new drugs can play an important role in solving the problems of in-stent thrombosis and perioperative bleeding. Currently, however, there are no data on these medications to be used in patients during hybrid revascularization.

One of the important issues in the modern cardiac surgery is whether robotic and endoscopic techniques are required for hybrid intervention. Robotic technology makes it possible to graft the left internal thoracic artery using endoscopic approach only. One study compared the surgical results of interventions with and without robotic techniques. The hybrid surgery group where the robotic technique was used had significantly better results, i.e.: shorter in-hospital stay, lower risk of bleeding, and early return to work. The 5-year survival rate was 92.9% and adverse cardiovascular events-free survival rate was 75.2%. The results of endoscopic surgery for single-vessel lesion are excellent, nevertheless this type of minimally invasive surgery is considered quite difficult, laborious and time-consuming (46–48).

An important aspect when different surgical options are compared is speed of recovery and return to normal physical activity and/or work. Kon et al. reliably demonstrated that hybrid surgery is an independent predictor of more rapid recovery and return to normal lifestyle (49).

The graft patency determined immediately after completion of the surgery was one of the characteristics of the safety and efficacy of hybrid technology (n = 112) compared with conventional CABG (n = 254). There were no significant differences in the graft dysfunction (2.8% in the hybrid surgery group and 3.4% in the CABG group) (50). Serruys and Holzhey reported that the survival rate and incidences of major cardiac and cerebral complications related to conventional CABG and hybrid surgery are similar (51, 27).

N. Bonaros et al. published interesting data summarizing the reported experience of hybrid interventions from 29 sites. Totally, 774 patients operated from 1996 to 2009 were analyzed. Overall mortality was 1.2%, 6-month mammary graft stenosis was detected in 2.9% of cases, whereas stent restenosis was determined in 14.5% of cases. However, it should be noted that not all of the studies used drug-eluting stents (52).

Another study comparing the hybrid revascularization and OPCAB in multivessel lesions was conducted at USA site. Totally, 147 hybrid surgeries (MID CAB of the LAD + PCI of non-LAD stenoses) and 588 OPCAB surgeries were analyzed over 7 years (2003–2010). MACCE rates were comparable between groups (0.02% in each group); the number of blood transfusions was lower in the hybrid revascularization group, however, the number of repeated revascularization was significantly higher when hybrid technology was used (12.2% versus 3.7%, respectively, $p < 0.001$). The expected 5-year survival rates were similar in both groups (hybrid revascularization and OPCAB: 86.8% versus 84.3%, $p = 0.61$) (53).

Many issues related to hybrid revascularization are still unresolved: 1) role of the CAB MID in hybrid revascularization; 2) sequence of steps (what to do first: PCI or MID CAB); 3) antiplatelet regimen in hybrid revascularization; 4) efficacy and safety of hybrid revascularization compared to CABG and PCI during in-hospital period and long-term follow-up. To answer these questions, prospective randomized studies comparing three methods of revascularization (CABG, PCI, and hybrid revascularization) are required. The tasks will be solved only through close collaboration and cooperation of cardiologists, cardiac surgeons and interventional cardiologists.

The study "Hybrid REvascularization Versus Standards (HREVS)" (http://www.clinicaltrials.gov/ct2/show/NCT01699048) comparing three methods of myocardial revascularization was initiated at our site. The study design is presented below.

There is a prospective randomized study including patients with stable CHD and multivessel coronary lesions. Patients are assigned into three groups depending on the type of revascularization:

1. Hybrid revascularization (MID CAB to the LAD with subsequent PCI of the non-LAD vessels).
2. PCI with multivessel stenting.
3. Coronary artery bypass grafting.

The follow-up time points are Years 1, 3 and 5 after revascularization.

Inclusion criteria:

1. Multivessel coronary lesions with stenoses ⩾ 70% (2 or more epicardial coronary arteries).
2. I–III FC stable angina (CCS).
3. Asymptomatic patients with documented ischemia based on the results of stress-test or stress echocardiography.
4. The ability to perform any of the three options of surgical myocardial revascularization (CABG, hybrid strategy, PCI with multivessel stenting).
5. The consensus between the cardiac surgeon and interventional cardiologist on whether the patient meets all the inclusion and exclusion criteria.
6. Informed consent for participation in the study signed by a patient.

Exclusion criteria:

1. Acute coronary syndrome
2. Previous CABG
3. In-stent thrombosis/restenosis in history
4. Comorbidity with a high risk of complications if the revascularization strategies under study are used
5. Significant brachiocephalic lesions
6. Comorbidity limiting life expectancy (non-curative malignancy)
7. Long-term follow-up is impossible
8. Participation in another study
9. Dual antiplatelet therapy is impossible
10. Left ventricular aneurysm, heart valve diseases requiring surgical correction.

Angiographic exclusion criteria:

• Critical stenosis (>95%) of the large epicardial coronary arteries
• Left main coronary artery disease
• Occlusion of the significant coronary artery
• One-vessel lesion
• Side branch involved in bifurcation lesion of >2.0 mm in diameter, which can be affected with a stent implanted in the main vessel

Primary endpoints:

– Serious adverse cardiovascular events (death from any cause, myocardial infarction, stroke or transient ischemic attack, repeated myocardial revascularization).
– Interventional success (clinical and angiographic success without complications).

Secondary endpoints:

– "Negative clinical and anatomic changes in the target vessel" (composite endpoint including in-stent restenosis or in-graft stenosis in combination with one of the following clinical signs: death, MI, or repeat revascularization of the target vessel).
– Rates of in-stent restenosis and in-graft stenosis (angiographic stenosis >50% of stent/graft diameter).
– The residual ischemia based on the SPECT data (%).
– The incidence of early and persistent postoperative cognitive dysfunction, according to neuropsychological and electroencephalographic tests.

Obligatory conditions:

1. Identical second-generation drug-eluting stents with efficacy proved in multicenter trials (Xience) should be used in both groups.
2. The time period between MID CAB and PCI is 1–3 days (within one in-hospital stay).
3. Dual antiplatelet therapy with a loading dose of clopidogrel 300 mg should be started one day after MID CAB in the hybrid revascularization group and before PCI in the second group.

Thus, the hybrid revascularization strategy using MID CAB followed by DES implantation is the rational hybrid option for patients with multivessel disease. This approach has advantages of both revascularization methods. Currently, there are no clear recommendations on hybrid revascularization in patients eligible for CABG and PCI. European guidelines on myocardial revascularization – 2014 demonstrate the lack of consensus on the place of hybrid revascularization; in these guidelines the indications for hybrid procedures are IIB class, the level of evidence is C (experts' opinion) (54). Only prospective randomized studies will determine the place of the hybrid method among other options of myocardial revascularization.

References

1. Jeremias A., Kaul S., Rosengart T.K. et al. The impact of revascularization on mortality in patients with nonacute coronary artery disease. Am. J Med. 2009, 122, 152–161.
2. Serruys P.W., Morice M.C., Kappetein A.P. et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N. Engl. J. Med. 2009, 360, 961–972.
3. Farkouh M.E., Domanski M., Sleeper L.A. et al. Strategies for multivessel revascularization in patients with diabetes. N. Engl. J. Med. 2012, 367, 2375–2384.
4. Tatoulis J., Buxton B.F., Fuller J.A. Patencies of 2127 arterial to coronary conduits over 15 years. Ann. Thorac. Surg. 2004; 77:93–101.
5. Mehta R.H., Honeycutt E., Shaw L.K. et al. Clinical and angiographic correlates of short- and long-term mortality in patients undergoing coronary artery bypass grafting. Am. J. Cardiol. 2007, 100, 1538–1542.
6. Cameron A., Davis K.B., Green G., Schaff H.V. Coronary Bypass Surgery with Internal-Thoracic-Artery Grafts – Effects on Survival over a 15-Year Period. N. Engl. J. Med. 1996, 334, 216–220.
7. Hayward P.A., Buxton B.F. Contemporary coronary graft patency: 5-year observational data from a randomized trial of conduits. Ann. Thorac. Surg. 2007, 84, 795–799.
8. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. N. Engl. J. Med. 1996, 335, 217–225.
9. CASS Principal Investigators and their associates. Coronary artery surgery study (CASS): a randomized trial of coronary bypass surgery. Survival data. Circulation. 1983, 68, 939–950.
10. 2011 ACCF/AHA/SCAI Guideline for Coronary Artery Bypass Graft Surgery J. Am. Coll. Cardiol. 2011, 1; doi:10.1016/j. jacc.2011.08.009.
11. Girasis C., Garg S., Räber L. et al. SYNTAX score and Clinical SYNTAX score as predictors of very long-term clinical outcomes in patients undergoing percutaneous coronary interventions: a substudy of SIRolimus-eluting stent compared with pacliTAXel-eluting stent for coronary revascularization (SIRTAX) trial. Eur. Heart J. 2011, 32 (24), 3115–3127.
12. Benetti F.J., Ballester C., Sani G. et al. Video assisted coronary bypass surgery. J. Cardiac. Surg. 1995, 10, 620–625.
13. Calafiore A.M., Gianmarco G.D., Teodori G. et al. Left anterior descending coronary artery grafting via left anterior small thoracotomy without cardiopulmonary bypass. Ann. Thorac. Surg. 1996, 61, 1658–1665.
14. Puskas J., Cheng D., Knight J. et al. Off-pump versus conventional coronary artery bypass grafting: a meta-analysis and consensus statement from the 2004 ISMICS consensus conference. Innovations. 2005, 1, 3–27.
15. Kon Z.N., Brown E.N., Tran R. et al. Simultaneous hybrid coronary revascularization reduces postoperative morbidity compared with results from conventional off-pump coronary artery bypass. J. Thorac. Cardiovasc. Surg. 2008, 135, 367–375.
16. DeRose J.J. Current state of integrated “hybrid” coronary revascularization. Semin. Thorac. Cardiovasc. Surg. 2009, 21,229–236.
17. Dekose J.J., Balaram S.K., Ro C. et al. Mid-term results and patient perceptions of robotically assisted coronary artery bypass grafting. Int. Cardiovasc. Thorac. Surg. 2005, 4, 406–411.
18. Meharwal Z.S., Mishra Y.K., Kohli V. et al. Off-pump multivessel coronary artery surgery in high-risk patients. Ann. Thorac .Surg. 2002, 74 (4). 1353–1357.
19. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention J. Am. Coll. Cardiol. 2011, 7. doi:10.1016/j. jacc.2011.08.007.
20. Sawhney N., Moses J.W., Leon M.B. et al. Treatment of left anterior descending coronary artery disease with sirolimus-eluting stents. Circulation. 2004, 110, 374–379.
21. Weisz G., Leon M.B., Holmes Jr. D.R. et al. Two-year outcomes after sirolimus-eluting stent implantation: results from the Sirolimus-Eluting Stent in de Novo Native Coronary Lesions (SIRIUS) trial. J. Am. Coll. Cardiol. 2006, 47, 1350–1355.
22. Stettler C., Wandel S., Allemann S. et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. Lancet. 2007, 370, 937–948.
23. Ashby D.T., Dangas G., Mehran R. et al. Comparison of clinical outcomes using stents versus no stents after percutaneous coronary intervention for proximal left anterior descending versus proximal right and left circumflex coronary arteries. Am. J. Cardiol. 2002, 89, 1162–1166.
24. Kappetein A.P., Feldman T.E., Mack M.J. et al. Comparison of coronary bypass surgery with drug-eluting stenting for the treatment of left main and/or three-vessel disease: 3-year follow-up of the SYNTAX trial. Eur. Heart J. 2011, 32, 2125–2134.
25. Hlatky M.A., Boothroyd D.B., Bravata D.M. et al. Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials. Lancet. 2009, 373, 1190–1197.
26. Mohr F., Redwood S., Venn G. et al. TCT-43 Final five-year follow-up of the SYNTAX Trial: Optimal Revascularization Strategy in Patients with Three-vessel Disease. J. Am. Coll. Cardiol. 2012, 60, 17.
27. Holzhey D.M, Jacobs S., Morchalski M. et al. Minimally invasive hybrid coronary artery revascularization. Ann. Thorac. Surg. 2008, 86, 1856–1860.
28. Angelini G.D., Wilde P., Salerno T.A. et al. Integrated left small thoracotomy and angioplasty for multivessel coronary artery revascularization. Lancet. 1996, 347, 757–758.
29. Byrne J.G., Leacche M., Vaughan D.E., Zhao D.X. Hybrid cardiovascular procedures. J. Am. Coll. Cardiol. Intv. 2008, 459–68.
30. Vassiliades T.A. Jr., Reddy V.S., Puskas J.D. et al. Long-term results of the endoscopic atraumatic coronary artery bypass. Ann. Thorac. Surg. 2007, 83, 979–985.
31. Hayward P.A., Buxton B.F. Contemporary coronary graft patency: 5-year observational data from a randomized trial of conduits. Ann. Thorac. Surg. 2007, 84, 795–799.
32. McGinn J.T. Jr, Usman S., Lapierre H. et al. Minimally Invasive Coronary Artery Bypass Grafting: Dual-Center Experience in 450 Consecutive Patients. Circulation. 2009, 120, 78–84.
33. Poston R.S., Tran R., Collins M. et al. Comparison of economic and patient outcomes with minimally invasive versus

traditional off-pump coronary artery bypass grafting techniques. Ann. Thorac. Surg. 2008, 248 (4), 638–646.
34. Bucerius J., Gummert J.F., Borger M.A. et al. Stroke after cardiac surgery: a risk factor analysis of 16,184 consecutive adult patients Ann. Thorac. Surg. 2003, 75, 472–78.
35. Lapierre H., Chan V., Sohmer B. et al. Minimally invasive coronary artery bypass grafting via a small thoracotomy versus off-pump: a case-matched study Eur. J. Cardiothorac. Surg. 2011, 40, 804–810.
36. Holzhey D.M, Jacobs S., Morchalski M. et al. Minimally invasive hybrid coronary artery revascularization. Ann. Thorac. Surg. 2008, 86, 1861–1865.
37. Friedrich G.J., Bonatti J. Hybrid coronary artery revascularization – review and update 2007. Heart Surg. Forum. 2007, 10, 292–296.
38. Berger P.B., Kleiman N.S., Pencina M.J. et al. Frequency of major noncardiac surgery and subsequent adverse events in the year after drug-eluting stent placement results from the EVENT (Evaluation of Drug-Eluting Stents and Ischemic Events) Registry. JACC Cardiovasc Interv. 2010, 3, 920–927.
39. Kim J.H., Newby L.K., Clare R.M. et al. Clopidogrel use and bleeding after coronary artery bypass graft surgery. Am. Heart J. 2008, 156, 886–892.
40. Zhao D.X., Leacche M., Jorge M. Routine Intraoperative Completion Angiography After Coronary Artery Bypass Grafting and 1-Stop Hybrid Revascularization: Results From a Fully Integrated Hybrid Catheterization Laboratory/ Operating Room. J. Am. Coll. Cardiol. 2009, 53 (3), 232–241.
41. Hu S., Li Q., Gao P. et al. Simultaneous hybrid revascularization versus off-pump coronary artery bypass for multi-vessel coronary artery disease. Ann. Thorac. Surg. 2011, 91,432–438.
42. Hu S.S., Xiong H., Zheng Z. et al. Midterm outcomes of simultaneous hybrid coronary artery revascularization for left main coronary artery disease. Heart Surg. Forum. 2012, 15, 18–22.
43. Kiaii B., McClure R.S., Stewart P. et al. Simultaneous integrated coronary artery revascularization with long-term angiographic follow-up. J. Thorac. Cardiovasc. Surg. 2008, 136, 702–708.
44. Reicher B., Poston R.S., Mehra M.R. et al. Simultaneous "hybrid" percutaneous coronary intervention and minimally invasive surgical bypass grafting: feasibility, safety, and clinical outcomes. Am. Heart J. 2008, 155, 661–667.
45. Damman P., Woudstra P., Kuijt W.J. et al. P2Y12 platelet inhibition in clinical practice. J. Thromb. Thrombolysis. 2012, 33, 143–153.
46. Bonatti J., Schachner T., Bernecker O. et al. Robotic totally endoscopic coronary artery bypass: program development and learning curve issues. J. Thorac. Cardiovasc. Surg. 2004, 127, 504–510.
47. Bonatti J., Schachner T., Bonaros N. et al. Effectiveness and safety of total endoscopic left internal mammary artery bypass graft to the left anterior descending artery. Am. J. Cardiol. 2009, 104, 1684–1688.
48. Bonatti J., Schachner T., Bonaros N. et al. Simultaneous hybrid coronary revascularization using totally endoscopic left internal mammary artery bypass grafting and placement of rapamycin eluting stents in the same interventional session. The COMBINATION pilot study. Cardiology. 2008, 110, 92–95.
49. Kon Z.N., Brown E.N., Tran R. et al. Simultaneous hybrid coronary revascularization reduces postoperative morbidity compared with results from conventional off-pump coronary artery bypass J. Thorac. Cardiovasc. Surg. 2008, 135, 367–375.
50. Bachinsky W.B., Abdelsalam M., Boga G. et al. Comparative study of same sitting hybrid coronary artery revascularization versus off-pump coronary artery bypass in multivessel coronary artery disease. Interv. Cardiol. 2012, 25 (5), 460–468.
51. Serruys P.W., Morice M., Kappetein A.P. et al. Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease. N. Eng. J. Med. 2009, 360, 961–972.
52. Bonaros N., Schachner T., Wiedemann D. et al. Closed chest hybrid coronary revascularization for multivessel disease – current concepts and techniques from a two-center experience. Eur. J. Cardiothorac. Surg. 2011, 40, 783–787.
53. Halkos M.E., Vassiliades T.A., Douglas J.S. et al. Hybrid coronary revascularization versus off-pump coronary artery bypass grafting for the treatment of multivessel coronary artery disease. Ann. Thorac. Surg. 2011, 92 (5), 1695–1701.
54. 2014 ESC/EACTS Guidelines on myocardial revascularization. The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur. Heart J. 2014, 35, 2541–2619.

Interventional Treatment of a Patient with Acute Myocardial Infarction and Cerebrovascular Accident: Two Diseases – One Operating Room

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The possibility of managing the patients with cerebrovascular accidents with the use of interventional techniques by endovascular surgeons who specialize in emergency cardiological care.
Key words: *management of cerebrovascular accident, endovascular surgery, thrombus extraction.*

Purpose. To demonstrate the feasibility of endovascular treatment of cerebrovascular accident in the cathlab of the department of cardiovascular surgery.

Material and methods. The authors present a clinical case of a patient admitted to the City Hospital № 79 within the first hours after the onset of acute myocardial infarction, and after 5 weeks – within the first hours after the onset of ischemic stroke. The patient underwent emergency coronary angiography, computed tomography, brain CT-perfusion, CT-angiography of intracranial arteries. Thrombus extraction was performed for the recovery of cerebral blood flow.

Results. Successful restoration of the blood flow in the previously occluded cerebral artery was beneficial for patient's neurological status

Conclusions. In order to improve the availability of this technique, the interventions on the cerebral arteries can be conducted by interventionists who specialize in cardiology, providing they possess necessary skills and appropriate surgical equipment.

Introduction

In Russia, over the last 10 years, cerebrovascular mortality rates firmly entrenched on the 2nd place after acute coronary pathology and amounted to 21.4%. More than 450,000 cerebrovascular accidents (CVA) are annually reported in Russia. 30-day and 1-year stroke mortality rates, according to various authors, range from 17 to 34% and 25-40%, respectively. Post-stroke disability is 3.2 per 10,000 population, only 20.2% of employees re-start working, and complete vocational rehabilitation, according to some data, is achieved only in 3–8% of cases (1, 2). Meanwhile, over the past 15 years CVA incidence markedly reduced in the Western Europe and USA on average by 7% per year and the mortality rate is only 12% versus 35% in Russia (2,3).

The mentioned statistical data suggest the need for further investigation and expansion of the options of CVA treatment proved to be effective in restoring cerebral blood flow. Intravenous thrombolysis, which many national guidelines relate to the class 1A, has relatively low efficacy. The artery recanalization rate varies from 10% in case of internal carotid artery (ICA) occlusion, up to 30% in case of middle cerebral artery (MCA) occlusion. Besides, the success of the CVA treatment is significantly limited by the time from disease onset and high incidence of hemorrhagic complications (4, 5).

In this connection, the interventional treatment options are of great interest; on one hand, they minimize the risk of hemorrhagic complications and give a high rate of successful recanalization (up to 91.2%) (6), but on the other hand, technical difficulty of these interventions should be noted as well as their low availability (4).

The main goal of treating patients with CVA is to restore cerebral blood flow as early as possible in order to save so-called "penumbra" –

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ischemic but still viable brain tissue. The therapeutic window for treatment of cerebral vascular accident is quite narrow and is less than 4.5 hours from the disease onset with intravenous thrombolytic therapy, while the interventional treatment options extend time frame up to 6 – 8 hours. It should be noted that only 1 to 7% of patients (!) in most countries worldwide are admitted within the time period suitable for reperfusion therapy. (7)

Another serious problem limiting wide application of interventional treatment options for cerebral vascular disorders is the lack of specialists – neuroradiologists. For example, in the USA in 2007, there were only 385 such specialists practicing in 238 hospitals in 45 states (8).

Thus, there were no such specialists in 5 states and the existing physicians (1.6 neuro-radiologists per hospital) are unable to provide 24/7 medical care for patients in need. (7)

The authors believe that if neuroradiologists as well as 24/7 specialist service (stroke center) are lacking, it is possible to provide interventional care for stroke patients in the institutions specializing in the treatment of coronary pathology. It is extremely important for an interventionist to possess appropriate skills and surgical equipment (6). The following clinical case may serve as a clear confirmation of this thesis.

Patient V., 78 y.o. It is known from his medical history that in 2008 he had ischemic CVA in the territory of the left MCA manifested as speech difficulties and right-sided hemiparesis. He was discharged in the satisfactory condition (Rankin score 2). Besides, patient suffers from permanent atrial fibrillation for a long time. In November 2014, he underwent emergency coronary angiography for non Q-wave anterior myocardial infarction in City Clinical Hospital No 79. Acute occlusion of the LAD orifice was detected (Rentrop collateral blood flow 1).

Mechanical recanalization and PTCA of the LAD were performed, and, given the diffuse pattern of LAD lesion, three stents were implanted: Tsunami Gold 3.0 x 15 mm and Tsunami Gold 3.0 × 20 mm in the proximal segment and Tsunami Gold 2.5 × 30 mm in the middle segment.

After stenting, the patient's condition became stable and on Day 11 the patient was discharged with the following recommendations: Brilinta 90 mg BID, Pradaxa110 mg BID, Carvedilol 6.25 mg BID, Simvastatin 40 mg.

After that, the patient's condition remained stable, he received the recommended medical therapy; however, 1 month and 9 days later he suddenly developed weakness in the left extremities.

He was admitted to City Hospital No 79 by ambulance 1 hour and 50 minutes after sudden loss of consciousness at home and fall.

On admission his condition was severe. Hemodynamics were stable: HR 80 bpm, BP 135/90 mm Hg.

Neurological status: the level of consciousness was reduced to deep stupor. There were no meningeal signs, tonic rightward turn of the head and the eyes and flattening of the left nasolabial fold were present. The patient had left-sided hemiparesis (scored up to 3 in the arm and leg). NIHSS score was 4, GCS score was 10.

Urgent native brain CT revealed left-sided cystic glial changes corresponding to previous CVA in the territory of the left MCA, however, there was no convincing evidence for a new cerebral vascular accident. Given the clinical signs of CVA, CT brain perfusion was performed (Omnipaque 350 – 50 ml intravenously). The comparison of the blood flow parameters in the area of interest (right parietal and temporal areas) with the opposite side revealed the data consistent with an ischemic CVA in the territory of the right MCA (Table 1).

To evaluate the extent of the brachiocephalic arteries lesions and provide urgent reperfusion therapy, the patient underwent angiography of the right common, external and internal carotid arteries, and right anterior, middle and posterior cerebral arteries. Acute occlusion of the right MCA from its orifice was revealed (Fig. 2 a). A neurological guidewire was introduced in the distal part of the MCA; a microcatheter was conducted over it (Fig. 2b), and angiography of the distal part of the artery was performed through this microcatheter. After that, thrombus extractor Catch+ was introduced and thrombus extraction was performed using two passages with a positive effect, thrombotic masses were aspirated. The restoration of the antegrade blood flow TICI III (Fig. 2 c) produced a positive effect on the clinical pattern manifested as significant regression of neurological symptoms already in the operating room – consciousness recovered, range of motion of the left limbs increased up to 4 points in the arm and 4.5 points in the leg.

Taking into account the presence of permanent form of atrial fibrillation, the absence of stenosis in the site of arterial occlusion, one could suggest, that the stroke had been caused by embolism, and not by in-situ thrombosis of the right MCA. It confirmed the importance not only of deaggregant, but also of anticoagulation therapy in post-PCI patients with ACS and atrial fibrillation. Safety and necessity

Table 1. Baseline parameters of the blood flow in the right and left hemispheres (brain CT perfusion)

	Right hemisphere	Left hemisphere
CVB (cerebral blood volume) Fig.1, a	2.7 ml/100 g	3.7 ml/100 g
CBF (cerebral blood flow) Fig.1, в	19.1 ml/100 g/min	60 ml/100 g/min
MTT (mean transit time) Fig. 1, с	10.2 sec	4.1 sec

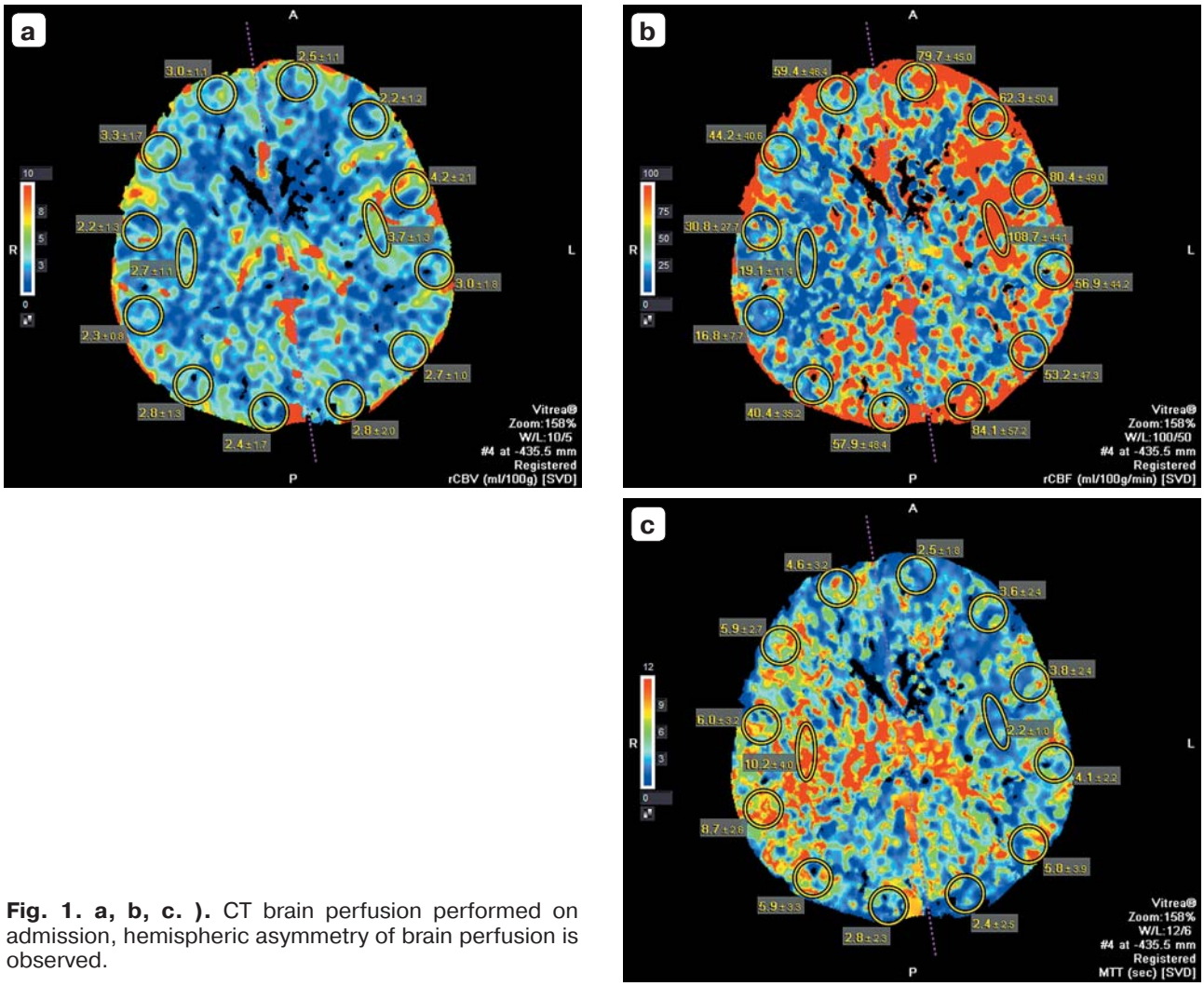

Fig. 1. a, b, c.). CT brain perfusion performed on admission, hemispheric asymmetry of brain perfusion is observed.

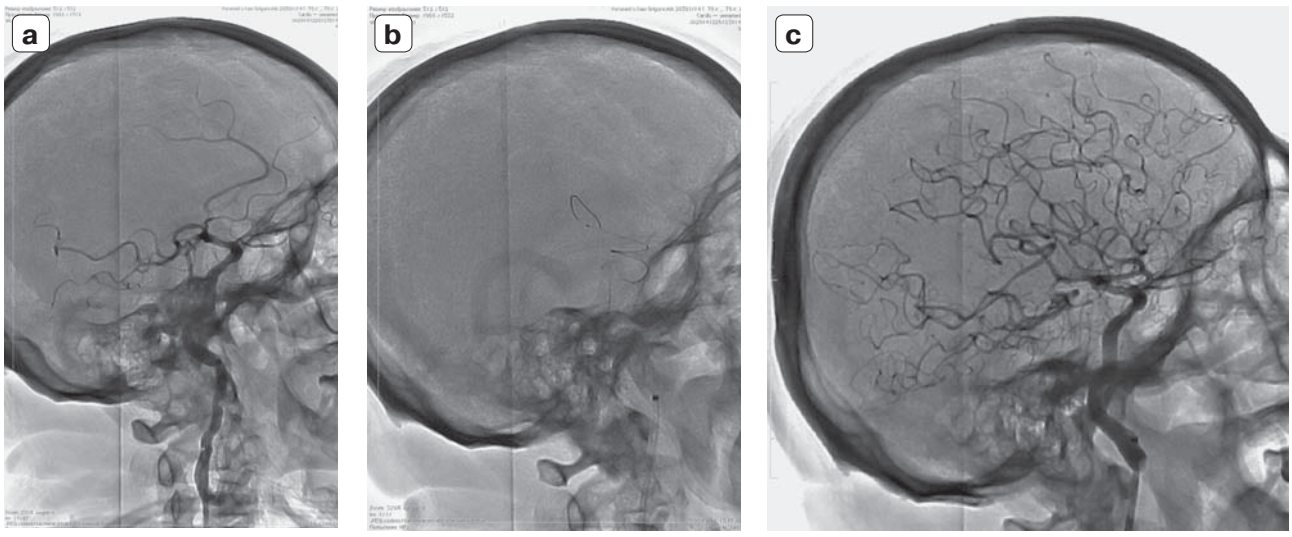

Fig. 2. a – baseline angiogram – occlusion of the right MBA. в – interventional step – introduction of Catch+ thrombus extractor. c – restored blood flow in the right MBA (TICI III).

Table 2. The parameters of the blood flow in the right and left hemispheres (brain CT perfusion) after blood flow restoration in the right MCA

	Right hemisphere	Left hemisphere
CVB (cerebral blood volume) Fig.3, a	1.6 ml/100 g	2.0 ml/100 g
CBF (cerebral blood flow) Fig.3, в	22.8 ml/100 g/min	30.2 ml/100 g/min
MTT (mean transit time) Fig. 3, с	4.2 sec	4.3 sec

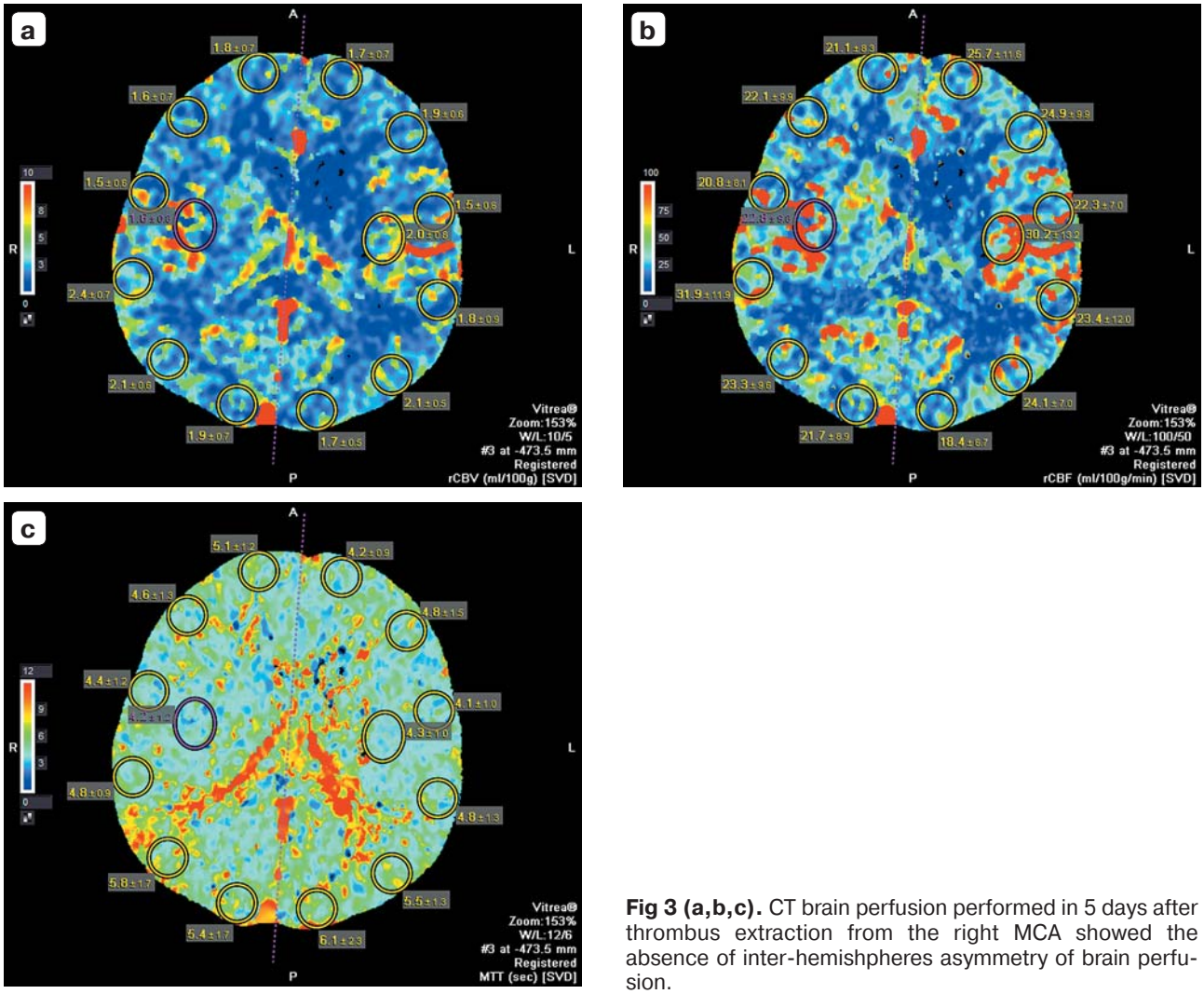

Fig 3 (a,b,c). CT brain perfusion performed in 5 days after thrombus extraction from the right MCA showed the absence of inter-hemishpheres asymmetry of brain perfusion.

of dual antiplatelet (related to previous LAD stenting) and anticoagulant therapy (for the prevention of thromboembolic complications in the presence of atrial fibrillation) were discussed. The risk of recurrent stroke in a patient with atrial fibrillation based on CHA2DS2-VASc scale was considered as high (score 6), the risk of bleeding according to HAS-BLED scale was also high (score 4). For this reason, a single-agent desegregation therapy was prescribed – Brilinta 90 mg BID without aspirin. Pradaxa 110 mg BID was prescribed for anti-coagulation therapy. In addition, the patient was treated with:Mexidol, Actovegin, Glycine, Bisoprolol, Enalapril.

A tendency for decreasing neurological deficit, normalization of cerebral blood flow, observed already in early postoperative period, was confirmed by CT brain perfusion on Day 5 after the procedure. The study revealed marked positive changes, namely improved perfusion in the areas of interest (the right temporal and parietal areas), reduced hemispheric asymmetry of blood flow (Figures 3 a,b,c, and Table 2).

On Day 15 after the admission the patient was discharged in stable condition. Neurological status at the time of discharge: satisfactory condition, conscious, sociable, and oriented. No face asymmetry. Dysarthria. The tendon reflexes are brisk on

the right. Increased spastic muscle tone in the right extremities. No focal left-sided pyramidal signs. Rankin score 2.

Conclusion

Currently, the interventional options are not first-line in the treatment of CVA, primarily due to low availability of this type of treatment. One way to overcome this, as suggested by some experts (4), is to involve a large group of physicians – interventional cardiologists providing 24/7 treatment of myocardial infarction. A necessary prerequisite is an appropriate training of so-called "multidisciplinary" specialists (7). In this context, the following global data reflecting the statistics of carotid stenting are very indicative: 58% of interventions are performed by interventional cardiologists, 25% by radiologists, and only 17% by cardiovascular surgeons (9).

It is quite likely that the combined efforts of these professionals will change the situation in the treatment of cerebral vascular disorders.

References

1. Feigin V.L., Lawes C.M.M., Bennet D.A., Anderson C.A. Stroke epidemiology: a review of population-based studies of incidence, prevalence, and casefatality in the late 20th century. Lancet Neurol. 2003, 2, 43–53.
2. Stulin I.D., Musin R.S., Belousov Yu.B. Stroke from the point of view of the evidence-based medicine. Kachestvennaya klinicheskaya praktika (Good Clinical Practice), 2003, 4, 10–18. (in Russian)
3. Varakin Yu.A. Epidemiological aspects of prevention of cerebrovascular accidents. Atmosphere. Nervous diseases, 2005, 2, 4–9 (In Russian).
4. Khripun A.V., Malevanny M.V. et al. First experience of the regional vascular center "Rostov Regional Clinical Hospital" in endovascular treatment of ischemic cerebrovascular accident. International Journal of Interventional Cardiology, 2010, 23, 32–42.
5. Gusev E.I., Skvortsova V.I., Martynov M.Yu. Management of patients in the acute phase of stroke. Vrach (Physician), 2003, 3, 18–24. (in Russian)
6. Nakano S., Iseda T., Yoneyama T. et al. Direct percutaneous transluminal angioplasty for acute middle cerebral artery trunk occlusion: an alternative option to intra-arterial thrombollysis. Stroke. 2002, 33, 2872–2876.
7. White J., Cates Ch., Cowley M. et al. Interventional stroke therapy: current state of the art and needs assessment. Catheter. Cardiovasc. Interv. 2007; doi: 10.1002/ccd: 1–7
8. Suzuki S., et al. Access to intra-arterial therapies for acute ischemic stroke: an analysis of the US population. Am. J. Neuroradiol. 2004, 25, 1802–1806.
9. Wholey M.H. et.al. Global experience in cervical carotid artery stent placement. Catheter. Cardiovasc. Interv. 2000, 50, 160–167.

Our First Experience with Prostatic Artery Embolization via Transradial Access

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The clinical case of successful prostatic artery embolization via transradial access is presented. The main advantages of this vascular access compared to transfemoral access are described.

Key words: *prostatic artery embolization, transradial access, transfemoral access, benign prostatic hyperplasia.*

Abbreviations

BPH – benign prostatic hyperplasia
LUTS – lower urinary tract syndrome
TURP – transurethral resection of the prostate
PAE – prostatic artery embolization
OUR – acute urinary retention
TRUS – transrectal ultrasound

Introduction

Benign prostatic hyperplasia (BPH) is the most common benign neoplasia in men. According to epidemiological studies, BPH prevalence in men aged from 60 to 69 y.o. is 50%, increasing to 90% in the people aged over 80 y.o. (1).

The main clinical manifestation of BPH is a lower urinary tract syndrome (LUTS). According to numerous studies, more than a half of BPH patients have a significant decrease in their quality of life due to LUTS (2–4).

The available international guidelines present algorithms optimizing the choice of treatment for BPH patients. It should be noted that medical therapy is the first-line treatment in the vast majority of routine clinical situations (α1-adrenoblockers and 5-α-reductase inhibitors) and surgical intervention should be considered only in cases of insufficient regression of clinical manifestations of LUTS or development of severe side effects (5).

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To date, a large number of various surgical, including minimally invasive, methods of BPH management based on mechanical (transurethral resection of the prostate, open prostatectomy) or physical effects (transurethral microwave vaporization, laser thermoablation) are developed. Among these interventions, the greatest evidence base is accumulated for open prostatectomy and transurethral resection of the prostate (TURP).

Currently, TURP, due to its high safety and low incidence of long-term relapses, is recognized as the "gold standard" for treatment of patients with LUTS caused by BPH if their prostate volume is up to 100 ml[3]. Open prostatectomy is preferable in case of larger prostate volume. However, these surgical interventions have their own serious disadvantages and complications.

Prostatic artery embolization (PAE) is a relatively new approach in the treatment of BPH patients. Initially, this intervention was designed to stop bleeding after prostate biopsy, adenoma- and prostatectomy (6–8).

In 2000 J. DeMeritt (9) was the first to propose PAE for reduction of the prostate volume, and only 10 years later F. Carnevalle published the first results of PAE performed in a BPH patient (10).

The therapeutic effect of PAE consists in ischemic necrosis of the prostate glandular tissue, which lowers its volume and reduces intensity of the LUTS signs (11).

The efficacy of PAE has been evaluated in several, mostly prospective, nonrandomized single centre studies. Based on meta-analysis performed by S. Schreuder et al., PAE contributes to significant decrease in the prostate volume, improvement of the objective uro-

dynamics parameters, and reduction of LUTS severity (12).

PAE is traditionally performed via right transfemoral access. This vascular access usually allows selective catheterization of both prostatic arteries. However, in some cases, the anatomical and morphological bifurcation patterns of the abdominal aorta and internal iliac arteries preclude this; therefore, puncturing of contralateral femoral artery is required. In addition, these circumstances often interfere with complete bilateral PAE, thereby reducing the clinical efficacy of this intervention (13–15).

Alternative arterial access for PAE described in the literature is brachial or axillary access. However, vascular access complications associated with this type of interventions are among the most common ones.

Transradial access significantly reduces the incidence of vascular access complications. It is widely used to perform coronary interventions; moreover, currently it is increasingly used for uterine artery embolization. The experience obtained from internal iliac artery catheterization via transradial access demonstrates the possibilities to simplify the procedure, reduce the risk of possible complications related to vascular access, achieve early activation of a patient, and increase post-procedural patient's comfort (16–18). We have found no information on use of this access for PAE in the available literature. A clinical case of successful transradial access for PAE is presented to your attention.

Clinical case

Patient A., 67 y.o. was admitted to BUZOO GK BSMP No.1, Omsk, in August 2014 with clinical signs of acute urinary retention (AUR). It is known from his medical history that he has long been suffering from LUTS caused by BPH for which he has been receiving tamsulosin and finasteride. For emergency indications, he underwent urethral draining and Foley catheter was placed. Transrectal ultrasound (TRUS) revealed unstructured, homogeneous prostate gland with increased volume up to 122 cm^3. Given increased serum titer of prostate-specific antigen up to 12.9 ng/ml, the prostate biopsy was performed to exclude prostatic cancer; it confirmed non-specific chronic prostatitis and prostate adenoma. The severity of inappropriate urination was assessed using IPSS (International Prostate Symptom Score) with a score of 24.

Given the AUR episode with the optimal medical therapy, inability to perform TURP, high risk of open prostatectomy, the collective decision was made to perform elective PAE.

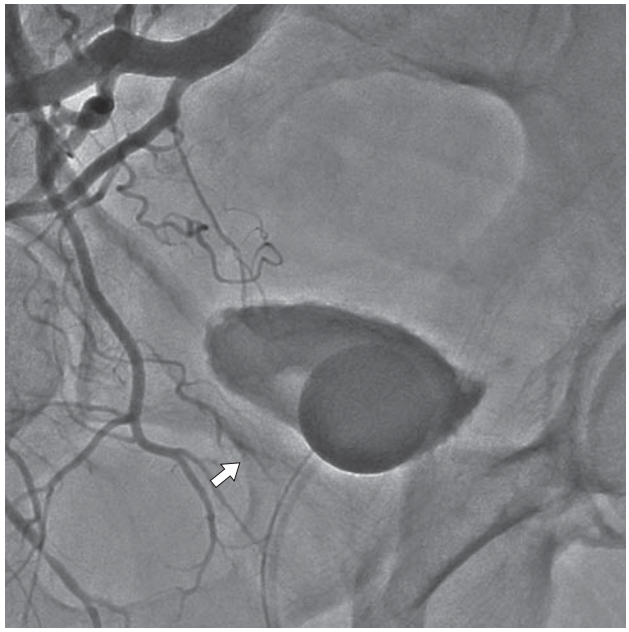

Figure 1. Angiogram of the right internal iliac artery: right prostatic artery (black arrow).

Left radial artery was punctured by Seldinger's technique and 6F sheath (Prelude, Merit Medical) was placed. To prevent spasm and occlusion of the radial artery, heparin 5000 IU, nitroglycerin 250 μg, and verapamil 2.5 mg were intraarterially injected through the sheath. To determine the anatomical patterns of the iliac arteries, the diagnostic catheter Pigtail was placed in the abdominal aorta above the bifurcation of the common iliac arteries, and diagnostic angiography was performed.

Diagnostic catheter Judkins Right 3.5 (length 125 cm, diameter 6 Fr, Performa, Merit Medical) was placed over the standard diagnostic guidewire 0.035" at the level of the abdominal aorta bifurcation. The tip of the diagnostic catheter was rotated to the right, and the right common and internal iliac arteries were subsequently catheterized followed by angiography of the right internal iliac artery to determine the origin of the right prostatic artery (Figure 1). The right prostatic artery was selectively catheterized using Maestro microcatheter (diameter 2.8 Fr, length 150 cm, the shape of the tip 45°, Merit Medical) and microguidewire Tenor (diameter 0.014", length 165 cm, Merit Medical) and its angiography was performed (Figure 2). Then, it was embolized using EmboSphere microspheres (diameter 100–300 μm, Merit Medical). The control angiogram revealed the blood flow only in the proximal part of the right prostatic artery, the distal arterial vasculature was dramatically depleted (Figure 3).

The next stage was the placement of the diagnostic catheter Judkins Right 3.5 at the level of the abdominal aorta bifurcation again. The tip of the diagnostic catheter was rotated to the left, and the

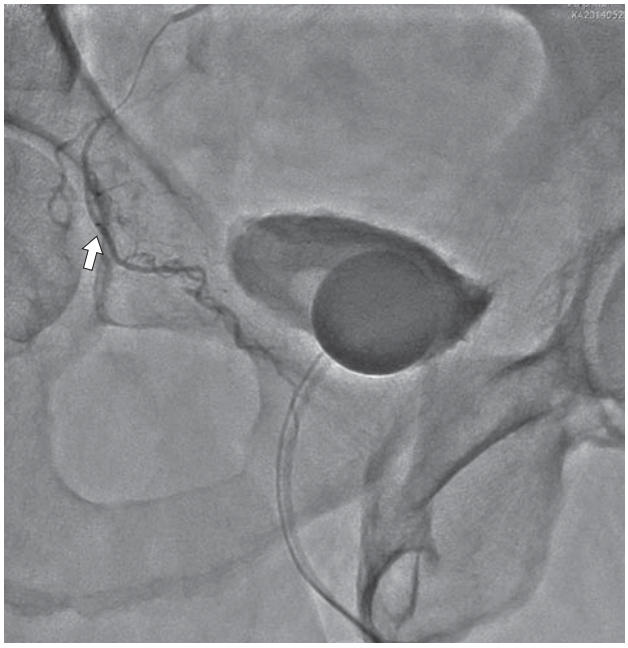

Figure 2. Angiogram of the right prostatic artery performed through the Maestro microcatheter: distal end of the microcatheter (arrow).

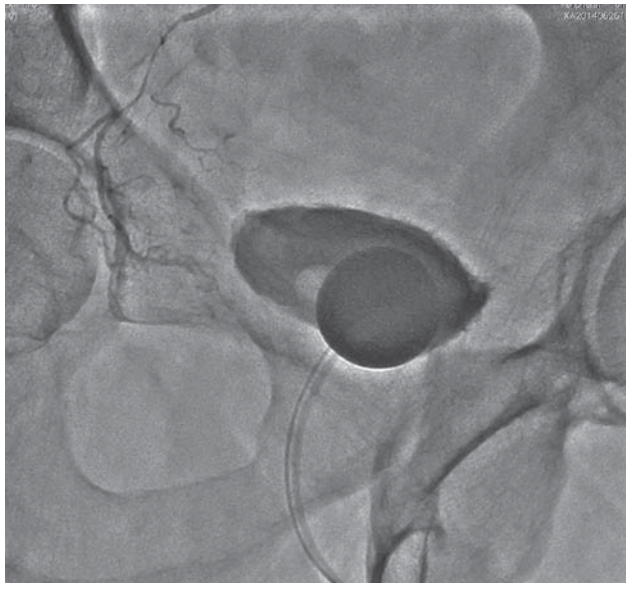

Figure 3. Total embolization of the right prostatic artery with the Embosphere microspheres.

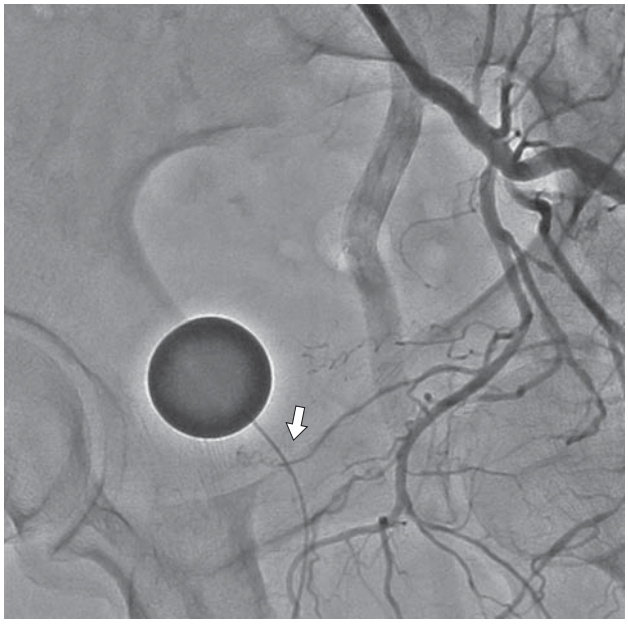

Figure 4. Angiogram of the left internal iliac artery: left prostatic artery (arrow).

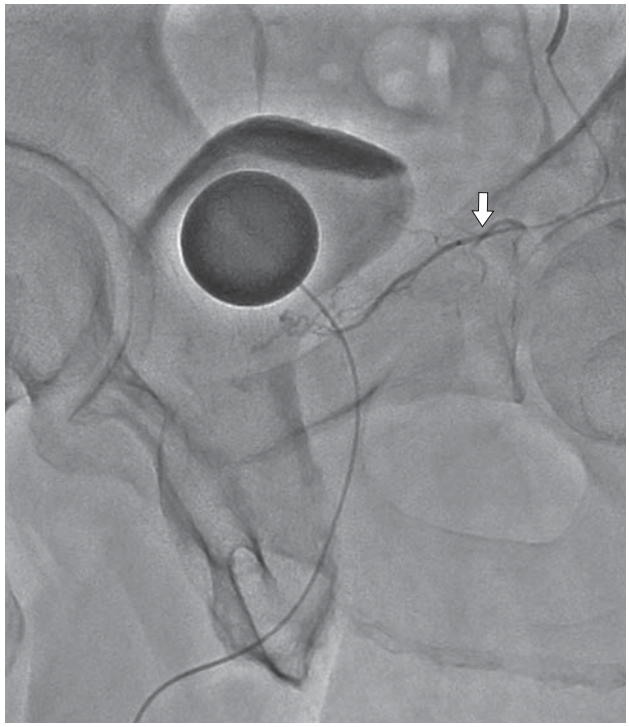

Figure 5. Angiogram of the left prostatic artery performed through the Maestro microcatheter: distal end of the microcatheter (arrow).

left common and internal iliac arteries were subsequently catheterized followed by angiography of the left internal iliac artery to determine the origin of the left prostatic artery (Figure 4). The left prostatic artery was selectively catheterized using Maestro microcatheter and microguidewire Tenor and its angiography was performed (Figure 5). Then, it was embolized using 100–300 μm EmboSphere microspheres. The control angiogram revealed the blood flow only in the proximal part of the left prostatic artery, the distal arterial vasculature was dramatically depleted (Figure 6). The microcatheter, diagnostic catheter, and sheath were subsequently removed. Finale (Merit Medical) – a radial compression device was placed over the puncture site.

Endovascular PAE lasted 54 minutes; the time spent on catheterization of the right and left prostatic arteries from the beginning of the left radial artery puncture was 36 minutes; radiation exposure was 0.51 mSv. Duration of post-procedural bed rest was

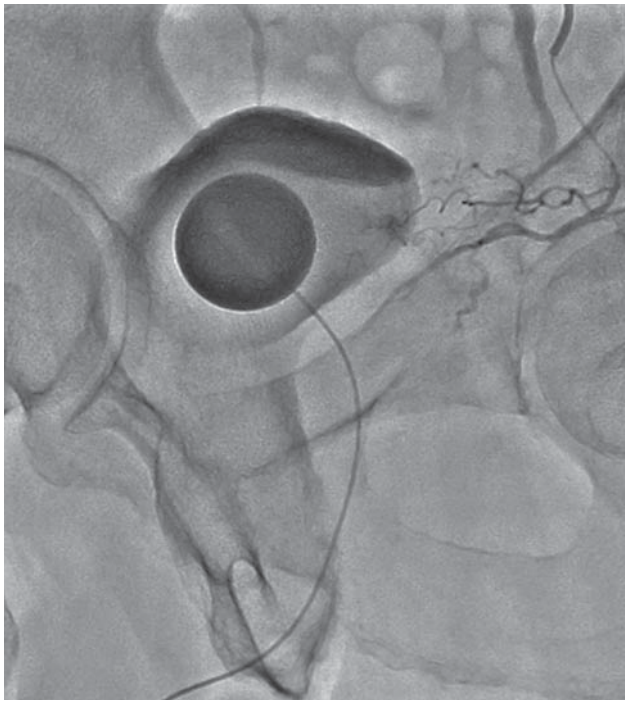

Figure 6. Total embolization of the left prostatic artery with the Embosphere microspheres.

1 hour. The radial compression device (Finale) was removed from the puncture site 6 hours after intervention. There were no complications related to the radial artery puncture site.

Post-interventional patient's condition has improved, and the control TRUS performed on Day 7 after PAE revealed reduction of the prostate volume to 104 cm^3. LUTS manifestations assessed using IPSS were relieved by 30% (to a score of 16).

Conclusion

Transradial access for PAE was applied for the first time. This access is relatively easy to perform and less invasive compared with the transfemoral one. It facilitates catheterization of the prostatic arteries, shortens procedural time and reduces X-ray exposure to the patient. Moreover, this access can significantly reduce the incidence of the vascular access complications, improve patient's comfort after intervention and allows activation of patients shortly after procedure. Thus, the described transradial access for PAE may be of great clinical significance.

References

1. Lee C., Kozlowski J.M., Grayhack J.T. Intrinsic and extrinsic factors controlling benigh prostatic growth. Prostate. 1997, 31(2), 131–138.
2. Wei J.T., Calhoun E., Jacobsen S.J. Urologic disease in America project: benign prostatic hyperplasia. J. Urol. 2005, 173 (4), 1256–1261.
3. Emberton M., Andriole G.L., de la Rosette J. et al. Benign prostatic hyperplasia. A progressive disease of aging men. Urology. 2003, 61 (2), 267–273.
4. Ziada A., Rosenblum M., Crawford E.D. Benign prostatic hyperplasia: An overview. Urology. 1999, 53, 1–6.
5. American Urological Association and European Association of Urology guidelines in the management of benigh prostatic hypertrophy: revisited. Curr. Opin. Urol. 2012, 22 (1), 34–39.
6. Appleton D.S., Sibley G.N., Doyle P.T. Internal iliac artery embolisation for the control of severe bladder and prostate haemorrhage. Br. J. Urol. 1988, 61 (1), 45–47.
7. Michel F., Dubruille T., Cercueil J.P. et al. Arterial embolization for massive hematuria following transurethral prostatectomy. J. Urol. 2002, 168 (6), 2550–2551.
8. Rastinehad A.R., Caplin D.M., Ost M.C. et al. Selective arterial prostatic embolization (SAPE) for refractory hematuria of prostatic origin. Urology. 2008, 71 (2), 181–184.
9. DeMeritt J.S., Elmasri F.F., Esposito M.P. et al. Relief of benign prostatic hyperplasia-related bladder outlet obstruction after transarterial polyvinyl alcohol prostate embolization. J. Vasc. Interv. Radiol. 2000, 11 (6), 767–770.
10. Carnevale F.C., Antunes A.A., da Motta Leal Filho J.M. et al. Prostatic artery embolization as a primary treatment for benign prostatic hyperplasia: preliminary results in two patients. Cardiovasc. Intervent. Radiol. 2010, 33 (2), 355–361.
11. Camara-Lopes G., Mattedi R., Antunes A.A. et al. The histology of prostate tissue following prostatic artery embolization for the treatment of benign prostatic hyperplasia. Int. Braz. J. Urol. 2013, 39 (2), 222–227.
12. Schreuder S.M., Scholtens A.E., Reekers J.A. et al. The role of prostatic arterial embolization in patients with benigh prostatic hyperplasia: a systematic review. Cardiovasc. Intervent. Radiol. 2014, 37 (5), 1198–1219.
13. Worthington-Kirsch R.L., Andrews R.T., Siskin G.P. et al. Uterine fibroid embolization: technical aspects. Tech. Vasc. Interv. Radiol. 2002, 5, 17–34.
14. Carnevale F.C., da Motta-Leal-Filho J.M., Antunes A.A. et al. Quality of life and symptoms relief support prostatic artery embolization for patients with acute urinary retention due to benign prostatic hyperplasia. J. Vasc. Interv. Radiol. 2012, 24, 535–542.
15. BilhimT., Pisco J., Rio Tinto H. et al. Unilateral versus bilateral prostatic arterial embolization for lower urinary tract symptoms in patients with prostate enlargement. Cardiovasc. Intervent. Radiol. 2013, 36 (2), 403–411.
16. Mclvor J., Rhymer J.C. 245 transaxillary arteriograms in arteriopathic patients: success rate and complications. Clin. Radiol. 1992, 45 (6), 390–394.
17. Jolly S.S., Yusuf S., Cairns J. et al. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. Lancet. 2011, 377 (9775), 1409–1420.
18. Khayrutdinov E.R., Vorontsov I.M., Arablinskiy A.V. Advantages of transradial access in urinary artery embolization. Diagnosticheskaya I interventsionnaya radiologia (Diagnostic and interventional radiology), 2015, 9 (1), 64–70. (in Russian)

Prevalence, Determinants and Prognostic Value of Contrast-induced Acute Kidney Injury after Primary Percutaneous Interventions

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Purpose of study: *to determine the incidence, the predictors and prognostic value of contrast-induced acute kidney injury (CIAKI) in patients with ST-elevation acute coronary syndrome (STE-ACS) after primary percutaneous coronary intervention.*

Material and methods. *CIAKI incidence was estimated using KDIGO 2012 criteria in 216 patients who were admitted to the hospital with STE-ACS and received PPCI (mean age 64 ± 13 years, arterial hypertension in 90%, history of MI in 27%, chronic kidney disease in 7%, diabetes mellitus type 2 in 21%). Logistic regression analysis was used to determine predictors of CIAKI. Patient prognosis was evaluated after 30 days and 12 months using telephone inquiry.*

Results. *CIAKI was diagnosed in 43 patients (20%); stage I in 81% and stage II in 19%. Patients with CIAKI were older (69 ± 13 and 63 ± 12 years, p <0.01), their baseline serum creatinine level was higher (104 ± 31 and 87 ± 22 μmol/l, p <0.001) as were the amount of contrast medium (CM) (282 ± 94 ml and 236 ± 85 ml, p <0.05) and CM volume to glomerular filtration rate (GFR) ratio (4.02 ± 2.15 and 2.32 ± 1.08, p <0,05), and left ventricle ejection fraction (LVEF) was lower (37 ± 10 and 41 ± 14%, p <0,05). Following independent predictors of CIAKI were revealed (listed according to their importance): CM volume to GFR ratio ⩾5.3, chronic kidney disease (CKD), in-hospital admission of nephrotoxic antibiotics, baseline GFR ⩽ 56.6 ml/min/1,73m^2, in-hospital admission of loop diuretics, multivessel disease, LVEF ⩽39.5%, CM volume ⩾250 ml, baseline serum creatinine level ⩾114 μmol/l, age ⩾65.5 years, in-hospital admission of mineralocorticoid receptor antagonists. CIAKI was associated with adverse outcomes: higher 30-days mortality (10 and 3%), higher readmission rate due to cardiovascular diseases (66 and 46%).*

Keywords: *contrast-induced acute kidney injury, ST-elevation acute coronary syndrome, primary percutaneous coronary intervention.*

Abbreviations

CIAKI – contrast-induced acute kidney injury;
BP – blood pressure;
SCL – serum creatinine level;
GFR – glomerular filtration rate;
STE-ACS – *ST*-elevation acute coronary syndrome;
PCI – percutaneous coronary intervention.
PPCI – primary percutaneous coronary intervention;
CM – contrast medium

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Introduction

The number of endovascular interventions, mostly percutaneous coronary interventions using iodine-containing contrast medium (CM), is increasing last years. PCI is the key component of treatment of acute coronary syndrome (ACS) (1–3). However, safety issues are still actual. One of the most serious complications of PCI is contrast-induced acute kidney injury (CIAKI) due to CM nephrotoxicity (4–6).

CIAKI incidence varies from 2% to 19% (7–9). Absence of uniform diagnostic criteria before 2012 and differences in populations studied could possibly lead to such dispersion of data. Strict diagnostic criteria for previously used term “acute renal failure” were not determined (10). Concept of “acute kidney injury” was later proposed and RIFLE (Risk, Injury, Failure, Loss, End-stage renal failure) and AKIN (Acute Kidney Injury Network) (10–11) criteria were developed. KDIGO guidelines for diagnosis and treatment

Table 1. R. Mehran scale of CIAKI risk assessment

Risk factor	Points
Hypotension (systolic BP < 80 mm Hg)	5
Intra-aortic balloon pump	5
Heart failure (III–IV FC NYHA)	5
Age >75 years	4
Anemia (hematocrit <39% (male), <36%(female))	3
Diabetes mellitus	3
Contrast medium volume	1 point for each 100 ml
SCL>132,6 μmol/l	4
or	
GFR 40–60 ml/min/1,73 m^2	2
20–39 ml/min/1,73 m^2	4
<20 ml/min/1,73 m^2	6

FC NYHA – functional class of heart failure, New-York Heart Association.

of CIAKI were published in 2012. These guidelines use RIFLE and AKIN combined criteria and consider dynamic serum creatinine level (SCL) and/or diuresis speed (12). According to KDIGO 2012 criteria CIAKI is determined as increase in SCL by 26 μmol/l in 48 hours after CM admission if there are no other reasons (12).

Patients risk of CIAKI should be assessed before PCI using R. Mehran scale. It considers both patient-related and PCI-related risk factors. (Table 1) (13–16). The score <5 suggets low risk of CIAKI, 6-10 suggests intermediate risk, 11-16 is indicative of high risk, and score ⩾16 suggets a very high risk. With the increase of score, the risk of CIAKI rises exponentially. (16).

Problem of CIAKI is increasingly important because PCI is often performed in elderly patients with variety of comorbidities while endovascular interventions become more and more complex, sometimes multistage and require administration of considerable amount of contrast medium.

Data on the incidence and prognostic value of CIAKI in Russia are limited.

the purpose of our study was to determine incidence, predictors and prognostic value of CIAKI in patients with STE-ACS which received PPCI.

Material and methods

The study enrolled 216 patients who were urgently admitted to the hospital with STE-ACS and received primary PCI. STE-ACS was diagnosed according to national and international guidelines (2, 17). Non-ionic low osmolar contrast medium iohexol (Omnipaque 350) and non-ionic iso-osmolar contrast agent iodixanol (Visipaque 320) were used for primary PCI. Radial access route was used in 95%. Patients with non-STE-ACS, delayed PCI, stable CAD and elective PCI were not included into study.

STE-ACS was treated according to national guidelines (17). Routine CIAKI prevention was used.

Patients' age ranged from 36 to 69 years (mean age 64 ± 13), arterial hypertension was present in 90%, 27% had a history of MI, 7% had chronic kidney diseases, 21% – type 2 diabetes mellitus, 14% had anemia. Characteristics of patients are presented in Table 2.

GFR was assessed using CKD-EPI formula according to SCL (18). Additionally urea, electrolytes (K, Na, Cl), hemoglobin and blood glucose level were assessed. CIAKI was diagnosed if increase in SCL by 26 μmol/l in 48 hours or 1.5 times SCL increase in 7 days after PCI were seen. CIAKI stage was deter-

Table 2. Characteristics of patients with STE-ACS and PCI (n = 216)

Index	Value
Male, n (%)	143 (66)
Age, years (M ± SD)	64 ± 13 (36–89)
Body weight, kg	80 ± 14
Smoking, n (%)	106(49)
Arterial hypertension, n (%)	194 (90)
Chronic heart failure, n (%)	134 (62)
Diabetes mellitus, n (%)	46 (21)
Anemia, n (%)	31 (14)
Cerebrovascular disease, n (%)	30 (14)
Chronic kidney disease, n (%)	15 (7)
Chronic obstructive pulmonary disease, n (%)	84 (39)
Liver disease, n (%)	9 (4)
Peripheral vessel disease, n (%)	1 (0.5)
Coronary angiography data	
Intact coronary arteries, n (%)	3 (1.7)
Stenosis <50%, n (%)	29 (13)
1 or 2 vessels diseased, n (%)	63 (29)
3 and more vessels diseased, n (%)	138 (64)
Left main coronary artery disease, n (%)	22 (10)

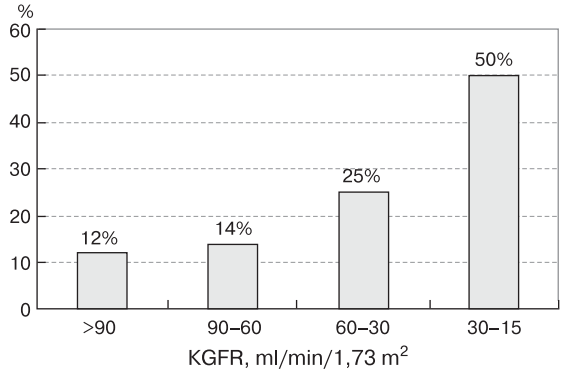

Fig. 1. Correlation between CIAKI incidence in patients with STE-ACS and PPCI and baseline GFR.

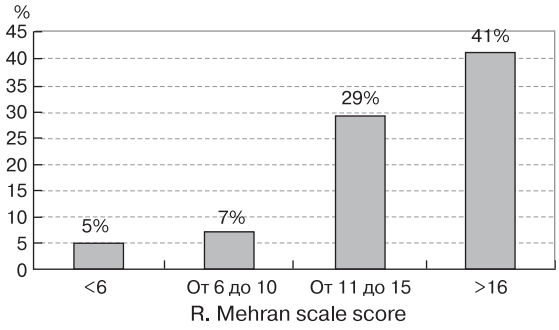

Fig. 2. Correlation between CIAKI incidence in patients with STE-ACS and PPCI and R. Mehran scale score.

mined according to RIFLE and AKIN combined criteria (12). Patient prognosis was evaluated after 30 days and 12 months using telephone inquiry (readmission, death).

Statistical analysis

Statistical analysis was performed using Statistica 8.0 for Windows using the standard algorithms of variational statistics. Arithmetic average and standard deviation were calculated for the quantitative values. Data is presented as M ± SD, where M is the mean value, SD – standard deviation of the average value. Paired two-sample Student's *t*-test was used to compare the average values. Qualitative variables are characterized by absolute (n) and relative (%) values. Chi-square test (χ^2) was used for comparison of frequencies of traits and qualitative variables. Mann–Whitney U-test was used to assess significance of differences between groups. Spearman rank correlation coefficient was calculated as a nonparametric measure of statistical dependence. The differences of average values and correlations were considered significant at $p < 0.05$.

Results of study

CIAKI was diagnosed in 43 (20%) patients – stage I in 81% and stage II in 19%.

CIAKI was more likely to develop in patients with lower baseline GFR (Fig. 1) and higher risk score according to R. Mehran scale (Fig. 2).

The groups of patients were comparable in gender and comorbidities incidence, except for higher CKD rate in CIAKI group – 21 and 3.5%, $p < 0.001$. CIAKI patients were older (69 ± 13 and 63 ± 12 years, $p < 0.01$), had higher baseline SCL (104 ± 31 и 87 ± 22 μmol/l, $p < 0.001$), more patients had higher (>10) R. Mehran scale score (44 and 25%, $p < 0.05$), lower LVEF (37 ± 10 and 41 ± 14%, $p < 0.05$).

CIAKI patients were significantly more likely to receive treatment by Verospiron (56 and 37%, respectively; $p < 0.05$), Furosemide (72 and 39%, $p < 0.05$) and nephrotoxic antibiotics (19 and 3.5%, $p < 0.05$). No statistically significant difference in Metformin, nonsteroidal anti-inflammatory drugs and ACE inhibitors administration rate was seen between two groups.

Besides, patients with CIAKI received larger volume of CM (282±94 ml and 236 ± 85 ml, $p < 0.05$), had higher incidence of multivessel disease (84 and 59%, $p < 0.05$) and higher CM volume to baseline GFR ratio (4.02 ± 2.15 and 2.32 ± 1.08, $p < 0.05$).

The curves obtained after constructing ROC models of the correlation between predictors and development of CI-AKI do not cross the control diagonal thus providing the sensitivity and specificity of >50%, area under the curve is >0.6 (indicating no less than satisfactory quality of model) at the level of statistical significance $p < 0.05$ (Table 3).

Table 3. Sensitivity and specificity of CIAKI predictors in patients with STE-ACS and PPCI

Index	AUC	Threshold value	Sensitivity, %	Specificity, %
Age, years	0,613	⩾ 65,5	63	65
Baseline SCL, μmol/l	0,589	⩾ 114	35	86
Baseline GFR, ml/min/1,73 m²	0,634	⩽ 56,6	54	81
CM volume, ml	0,727	⩾ 250	71	60
CM volume to GFR ratio	0,678	⩾ 5,3	51	77
LVEF, %	0,674	⩽ 39,5	71	63

Table 4. Predictors of CIAKI in patients with STE-ACS and PPCI

Index	Odds ratio	95% confidence interval	p
CM volume to GFR ratio ⩾5,3	7.90	3.19–19.40	<0.05
Chronic kidney disease	7.37	2.46–22.06	<0.001
Nephrotoxic antibiotics	6.36	2.08–19.49	<0.05
Baseline GFR ⩽56,6 ml/min/1,73 m^2	5.40	2.60–11.19	<0.05
Loop diuretics	3.98	1.92–8.30	<0.01
Multivessel disease	3.58	1.51–8.49	<0.05
LVEF ⩽39,5%	3.28	1.65–6.54	<0.05
CM volume ⩾250 ml	3.26	1.63–6.53	<0.05
Baseline SCL ⩾114 μmol/l	3.14	1.42–6.94	<0.05
Age ⩾65,5 years	2.80	1.40–5.59	<0.05
Antagonists of mineralocorticoid drugs	2.15	1.09–4.23	<0.05

Independent predictors of CIAKI after PPCI were determined using multivariate regression analysis (Table 4).

CIAKI group analysis showed greater 30-days mortality (χ^2 = 7.2, p < 0.05) and 6-month readmission rate (χ^2 = 3.1, p < 0.05) (Fig. 3).

Stage II of CIAKI was associated with higher adverse outcomes, both late and in-hospital. In-hospital mortality was 37.5% (0% for stage I), 30-days mortality was 37.5% (6.5% for stage I).

Discussion

Incidence, predictors and prognostic value of contrast-induced acute kidney injury (CIAKI) in patients with ST-elevation acute coronary syndrome (STE-ACS) who received primary percutaneous coronary intervention (PPCI) were assessed. The results highlight the existing problem of CIAKI after primary PCI. Timely diagnosis of CIAKI determines patient's treatment and prognosis.

Problem of CIAKI attracts even more attention along with the increasing incidence of cardiovascular disease, kidney disease, diabetes mellitus, obesity, growth of population lifespan and increasingly high number of endovascular procedures last years.

CIAKI is one of the most serious complications of PCI, especially in STE-ACS group. CIAKI is third among the causes of in-hospital acute kidney failure (first two are renal hypoperfusion and nephrotoxic drugs administration) and occurs in 3–19% of all PCI patients (7–9). It is considered that risk of CIAKI is low if renal function is intact, even in diabetes mellitus (1–2%) (20).

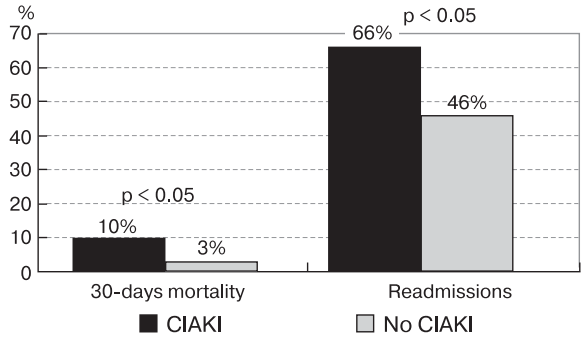

Fig. 3. Prognosis for patients with STE-ACS, PPCI and CIAKI.

However CIAKI incidence rises up to 25% in patients with impaired renal function, some risk factors (e.g. combination of CKD and diabetes mellitus, CHF, age, nephrotoxic drugs administration) (20).

Iodine-containing CM administration lead to significantly higher incidence of CIAKI in critically ill patients. SCL increase > 25% occurred in 18% of 75 patients from intensive care unit after CT scan with low osmolar CM (21) whereas no SCL increase occurred in patients which received CT scan without contrast medium administration.

Above mentioned dispersion of data is caused by difference in diagnostic criteria, different level of hospitals and differences in populations studied (22–24).

E.g. term "contrast-induced nephropathy" determined as increase in SCL ⩾0.5 mg/dl (⩾44 μmol/l) or 25% in 48 hours was widely used earlier (25). Sometimes SCL increase was assessed in 5 days after CM administration (26).

We determined the incidence of CIAKI as high as 20%, which is higher than in other studies. We link this to widespread comorbidity and unstable state of our STE-ACS patients.

Thus CIAKI incidence varies greatly depending on population studied and risk factors.

CIAKI predictors include 2 groups. First group relates to patient and includes CKD, low LVEF, baseline SCL, nephrotoxic drugs administration, loop diuretics, anti-mineralocorticoid drugs administration. Second group includes PCI-related factors (CM volume, multivessel disease, CMV/GFR ratio) (27–30).

Multiple studies showed that baseline renal function impairment is the most important risk factor of CIAKI. Since that renal function screening is highly recommended to diagnose acute and chronic kidney disease (12).

It should be noted that GFR value threshold associated with elevated risk of CIAKI is not defined.

Current study demonstrates that CIAKI is associated with adverse outcomes: greater 30-days mortality (10 and 3%), higher rate of readmissions (66 and 46%). Greater increase in SCL is associated with even higher mortality: 37.5% of patients with stage II of CIAKI died in hospital and 37.5% more in 30 days.

It is important to identify patients with high risk of renal function impairment as early as possible. Observational studies showed that CIAKI is associated with prolonged hospital stay, higher rate of readmissions, CKD progression, elevated cardiovascular and overall mortality (31–33). Results of large studies confirm CIAKI prognostic value (34–37).

Thus CIAKI after PCI is the predictor of adverse outcomes of STE-ACS, both early and late. Patient stratification according to R Mehran scale is needed along with precise monitoring of renal function in this patients' population to timely diagnose CIAKI and provide adequate prevention and treatment.

Conclusion

CIAKI (according to KDIGO 2012 criteria) develops in 20% of patients with STE-ACS and PCI, mainly within the first 48 hours after the intervention. CIAKI is more frequent in patients with lower baseline SCL and higher risk according to R. Mehran scale.

CIAKI development is associated with both patient-related and PCI-related factors.

CIAKI in patients with STE-ACS and PCI is associated with poor prognosis: higher 30-days mortality and higher readmissions rate.

Stratification of patients with STE-ACS and planned PPCI, monitoring of renal function, adequate prevention and treatment are needed.

References

1. Kume K., Yasuoka Y., Adachi H. et al. Impact of contrast-induced acute kidney injury on outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Cardiovasc. Revasc. Med. 2013, 14 (5), 253–257.
2. Steg P.G., James S.K., Atar D. et al. ESC Guidelines for themanagement of acutemyocardial infarction in patients presenting with ST-segment elevation: the Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). Eur. Heart J. 2012, 33, 2569–2619.
3. Domoradskaya A.I. Contrast-induced nephropathy: risk factors. Rossiysky elektronny jurnal radiologii (Ruaain e-journal of Radiology). 2011, 4, 27–32. (In Russian)
4. Volguina G.V. . Contrast-induced nephropathy: pathogenesis, risk factors, prevention strategy. Nefrologia i dializ (Nephrology and dialysis) 2006, 2, 176–183. (In Russian)
5. Dundua D.P. Contrast-induced nephropathy in interventional cardiology and angiology. Autoref. ... thes. Doctor med. Sci.. Moscow, 2010. (In Russian)
6. Belopukhov V.M., Yakupov I.F., Aynutdinova I.A., Ivanova A.Yu. Renal function disturbances in patients with myocardial infarction before and after percutaneous coronary interventions. Meditsinksy almanakh (Medical almanac) 2013, 4 (28), 55–56. (In Russian)
7. Tsai T.T., Patel U.D., Chang T.I. et al. Contemporary incidence, predictors, and outcomes of acute kidney injury in patients undergoing percutaneous coronary interventions: insights from the NCDR Cath-PCI registry. J. Am. Coll. Card. Cardiovasc. Interv. 2014, 7 (1), 1–9.
8. Watabe H., Sato A., Hoshi T. et al. Association of contrast-induced acute kidney injury with long-term cardiovascular events in acute coronary syndrome patients with chronic kidney disease undergoing emergent percutaneous coronary intervention. Int. J. Cardiol. 2014, 174 (1), 57–63.
9. Brown J.R., DeVries J.T., Piper W.D. et al. Serious renal dysfunction after percutaneous coronary interventions can be predicted. Am. Heart J. 2008, 155, 260–266.
10. Bellomo R., Ronco C., Kellum J. et al. Acute renal failure – definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit. Care. 2004, 8, 204–212.
11. Mehta R., Kellum J., Shah S. et al. Acute Kidney Injury Network (AKIN): report of an initiative to improve outcomes in acute kidney injury. Crit. Care. 2007, 11, R31.
12. KDIGO Clinical practice guideline for acute kidney injury. Kidney Int. 2012, 2 (1), 1–141.
13. Akrawinthawong K., Ricci J., Cannon L. et al. Subclinical and clinical contrast-induced acute kidney injury: data from a novel blood marker for determining the risk of developing contrast-induced nephropathy (ENCINO), a prospective study. Ren. Failure. 2014, 12, Early Online: 1–5.
14. Loh J.P, Pendyala L.K., Kitabata H. Comparison of outcomes after percutaneous coronary intervention among different coronary subsets (stable and unstable angina pectoris and *ST*-segment and non-*ST*-segment myocardial infarction). Am. J. Cardiol. 2014, 113 (11), 1794–1801.
15. Meinel F.G., Cecco C.N., Schoepf U.J., Katzberg R. Contrast-induced acute kidney injury: definition, epidemiology, and outcome. BioMed. Res. Intern. 2014, ID 859328, 6 p. http://www.hindawi.com/journals/bmri/2014/859328/
16. Mehran R., Aymong E.D., Nikolsky E. et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. J. Am. Coll. Cardiol. 2004, 44, 1393–1399.
17. Ruda M.Ya., Golitsyn S.P., Gratsiansky N.A. et al. National guidelines of All-Russian Society of Cadriology with the angagement of the Ministry of Healthcare and Social devel-

opment on the diagnosis and treatment of ST-elevatiobn myocardial infarction. Kardiovasckularnaya terapia i profilaktika (Cardiovascular therapy and prophylactis) . 2007, 6 (8), suppl. 1: 415–500. (in Russian)
18. Levey A.S., Stevens L.A., Schmid C.H. et al. CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. Ann. Intern. Med. 2009, 150 (9), 604–612.
19. Berns A.S. Nephrotoxicity of contrast media. Kidney Int. 1989, 36, 730–740.
20. Rudnick M.R., Goldfarb S., Tumlin J. Contrast-induced nephropathy: is the picture any clearer? Clin. J. Am. Soc. Nephrol. 2008, 3, 261–262.
21. Polena S., Yang S., Alam R. et al. Nephropathy in critically Ill patients without preexisting renal disease. Proc. West Pharmacol. Soc. 2005, 48, 134–135.
22. Ronco C., Stacul F., McCullough P.A. Subclinical acute kidney injury (AKI) due to iodine-based contrast media. Eur. Radiol. 2013, 23 (2), 319–323.
23. Loh J.P., Pendyala L.K., Torguson R. Incidence and correlates of major bleeding after percutaneous coronary intervention across different clinical presentations. Am. Heart J. 2014, 168 (3), 248–255.
24. James M.T., Ghali W.A., Knudtson M.L. et al. Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) Investigators. Associations between acute kidney injury and cardiovascular and renal outcomes after coronary angiography. Circulation. 2011, 123, 409–416.
25. Harjai K.J., Raizada A., Shenoy C. et al. A comparison of contemporary definitions of contrast nephropathy in patients undergoing percutaneous coronary intervention and a proposal for a novel nephropathy grading system. Am. J. Cardiol. 2008, 101, 812–819.
26. From A.M., Bartholmai B.J., Williams A.W. et al. Sodium bicarbonate is associated with an increased incidence of contrast nephropathy: a retrospective cohort study of 7977 patients at mayo clinic. Clin. J. Am. Soc. Nephrol. 2008, 3, 10–18.
27. Davenport M. S., Khalatbari S., Cohan R.H. et al. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material: risk stratification by using estimated glomerular filtration rate. Radiology. 2013, 268 (3), 719–728.
28. Kim G.S., Ko Y.G., Shin D.H. et al. Elevated serum cystatin C level is an independent predictor of contrast-induced nephropathy and adverse outcomes in patients with peripheral artery disease undergoing endovascular therapy. Vasc. Surg. 2015, 0741-5214(14): 02228-9.
29. Lucreziotti S., Centola M., Salerno-Uriarte D. et al. Female gender and contrast-induced nephropathy in primary percutaneous intervention for ST-segment elevation myocardial infarction. Int. J. Cardiol. 2014, 174, 37–42.
30. McCullough P., Adam A., Becker C. et al. Risk prediction of contrast-induced nephropathy. Am. J. Cardiol. 2006, 98, 27–36.
31. Andreucci M., Faga T., Pisani A. et al. Prevention of contrast-induced nephropathy through a knowledge of its pathogenesis and risk factors. Scientific Wld J. 2014; http://www.hindawi.com/journals/tswj/2014/823169/ ID 823169, 16 pages.
32. Marenzi G., Lauri G., Assanelli E. et al. Contrast-induced nephropathy in patients undergoing primary angioplasty for acute myocardial infarction. J. Am. Coll. Cardiol. 2004, 44, 1780–1785.
33. Anderson H.V., Shaw R.E., Brindis R.G. et al. Risk-adjusted mortality analysis of percutaneous coronary interventions by American College of Cardiology/American Heart Association guidelines recommendations. Am. J. Cardiol. 2007, 99, 189–196.
34. Weisbord S., Chen H., Stone R. et al. Associations of increases in serum creatinine with mortality and length of hospital stay after coronary angiography. J. Am. Soc. Nephrol. 2006, 17, 2871–2877.
35. Iakovou I., Dangas G., Mehran R. et al. Impact of gender on the incidence and outcome of contrast induced nephropathy after percutaneous coronary intervention. J. Invasive Cardiol. 2003, 15, 18–22.
36. Schilp J., de Blok C., Langelaan M. et al. Guideline adherence for identification and hydration of high-risk hospital patients for contrast-induced nephropathy. BMC Nephrol. 2014, 15, 2.
37. Rynkowska-Kidawa M., Zielińska M., Chizyński K., Kidawa M. In-hospital outcomes and mortality in octogenarians after percutaneous coronary intervention. Kardiol. Pol. 2015. doi: 10.5603/KP.a2014.0247.

Acute Left Ventricular Failure in Patients with Type 2 Diabetes Mellitus

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The article presents a literature review on the prevalence, pathogenesis, and treatment of myocardial infarction (MI) complicated by acute left ventricular failure (ALVF) in patients with type 2 diabetes mellitus (T2DM). Diabetes mellitus contributes to reduction of myocardial contractility. Myocardial remodeling in T2DM is affected by combination of factors associated with diabetic cardiomyopathy, reduction of the metabolic activity of cardiomyocytes, insufficient glucose transport into cells, endothelial dysfunction, diabetic macro- and microangiopathy, myocardial fibrosis leading to disruption of left ventricle filling and development of ALVF. Modern pharmacological agents and interventions for MI increase the life span and improve the quality of life of T2DM patients. However, MI is complicated with ALVF 3 times as frequently and mortality related to acute MI is 2 times higher in T2DM patients compared to non-T2DM patients.

Key words: *type 2 diabetes mellitus, acute myocardial infarction, acute left ventricular failure.*

Cardiovascular diseases (CVDs) are the leading cause of patients' death in economically developed countries. In 2011 in the Russian Federation (RF), based on the Federal Service of State Statistics data, the number of CVDs patients was 22,692.2 per 100,000 population. 26% out of them died from coronary heart disease (CHD), which occupies a leading position in the CVD mortality worldwide (1). The number of patients suffering from type 2 diabetes mellitus (T2DM) doubles over each 10 years (2). In the Russian Federation, as of January 01, 2013, the number of DM patients was 3,778,000 and 3,452,000 out of them had T2DM (3). Type 2 diabetes mellitus is a chronic disease due to low biological activity of insulin which is the cause of serious complications and disability and is associated with vascular lesions of the heart, brain, extremities, kidneys, and retina. Coronary heart disease is the leading cause of mortality of T2DM patients due to atherosclerosis, macro- and microvascular lesions of coronary arteries. With 1% increase in glycated hemoglobin level, CVD risk increases by 10% (4). In T2DM men and T2DM women, CHD is revealed 2 and 3 times higher compared to general population (4). Thus, the rapidly growing population of T2DM patients in a short time will change the modern view of the improved prognosis for CVDs treatment.

Acute coronary syndrome (ACS) is a sudden clinical condition related to development of myocardial ischemia with typical constellation of clinical, biochemical and electrocardiographic changes and based on morphological disorders of coronary arteries patency and realized in acute myocardial infarction (AMI) or unstable angina (UA) (5, 6). In recent years, the AMI-related mortality in T2DM patients remains high (7). The American College of Cardiology (ACC) and American Heart Association (AHA) reports that mortality in AMI patients with T2DM has increased compared with non-T2DM patients (8). The study of AMI-related mortality showed that the patients with a history of T2DM died 3–4 times more frequently than those with normal carbohydrate metabolism (CM). The relationship between T2DM and mortality is high, even after adjustment for other CHD risk factors (smoking, hypercholesterolemia, physical inactivity) (9, 10). Therefore, despite modern methods of AMI treatment (thrombolytic therapy, angiosurgery), the mortality in T2DM patients remains 2–3 times higher compared to those with normal CM (1, 11, 12).

Based on literature data, it can be concluded that T2DM contributes a lot to the increased risk for AMI (11, 13) and incidence of its complications, namely pulmonary edema (14, 15), cardiogenic shock and acute left ventricular (LV) aneurysm (16, 17). This is explained by atherosclerotic lesions of the proximal and

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distal parts of coronary arteries in combination with "metabolic ischemia" of the cardiomyocytes (14, 15, 18), diabetic autonomic cardioneuropahy (DACN) (19), which occurs in patients with a long lasting T2DM and is a predictor of high mortality (20).

Currently, prevalence and treatment of AMI complicated with acute left ventricular failure (ALVF) are described in detail in the literature. Therefore, in recent years, the publications concerning ALVF in AMI patients are rare. However, this issue in T2DM patients should be analyzed, as AMI is more frequently complicated with ALVF in these patients (16). The course of fatal AMI in T2DM patients is fulminant. They die more frequently within the first hours of hospitalization, with ALVF and cardiogenic shock as the main causes of mortality (11, 21).

Acute left ventricular failure (pulmonary edema) is a syndrome that occurs suddenly and is characterized with fluid accumulation in the interstitium and pulmonary alveoli, followed by gas exchange disorder in the lungs and hypoxia manifested as skin cyanosis and choking. ALVF mechanisms are related to blood circulation disturbances and include increased pulmonary venous pressure without left ventricular failure (mitral stenosis); increased pulmonary venous pressure with left ventricular failure; increased pulmonary capillary pressure as a result of increased pressure in the pulmonary artery (pulmonary edema associated with excessive perfusion) (22). It is important to note that AMI is complicated with ALVF in T2DM patients 3 times as often as in patients with normal CM (23). The degree of congestion in the lungs depends on pressure in the left atrium (LA). Slightly increased pressure (18–20 mm Hg) in the LA leads to perivascular and peribronchial edema. Further increase in the LA pressure (>25 mm Hg) results to liquid penetration in the alveoli. Normally, only two thirds inhaled air, so called alveolar ventilation, reach alveoli. Without external breathing the human body can usually live for up to 5–7 minutes, with consequent loss of consciousness, irreversible changes in the brain and death. There are interstitial and alveolar pulmonary edemas. In case of interstitial pulmonary edema, the fluid does not extend beyond the peribronchial space. This clinical stage of edema manifests as progressive shortness of breath and cyanosis. In case of alveolar pulmonary edema, the fluid penetrates into the alveoli. It contains large amounts of protein, which mix with the inhaled air in the alveoli and form a foam that fills the airways, further reducing the alveolar ventilation. In the most severe cases, the foam comes out from the mouth and nose. Physical signs of alveolar pulmonary edema are rales, sometimes heard at a distance and associated with fluid penetration into the bronchial lumen (25).

Declined myocardial contractile capacity underlies ALVF in AMI patients. There are three myocardial areas determining cardiac pump function in AMI patients.

1) Necrotic area that no longer participates in the myocardial contractility. In case of acute LV aneurysm, some amount of blood flows in the aneurismal sac during systole, but this blood "pumping" is not usually large enough to affect cardiac output significantly. In T2DM patients, STEMI incidence is 10–15% (26) – 20% (27) higher compared to patients with normal CM. Myocardial necrosis area associated with infarct-related artery is by 10–15% larger in T2DM patients compared to non-T2DM patients (28, 29). Other studies demonstrate the same myocardial necrosis area in T2DM patients and those with normal CM (30, 31), however, in T2DM patients cardiogenic shock and pulmonary edema occur several times more often (13, 23). AMI pattern in T2DM patients is fulminant; the mortality rate within the first 6 hours after hospitalization achieves 26%, when only ischemic changes are observed in the myocardium and there is no necrosis of cardiomyocytes (11, 31); postmortem examination reveals morphological signs of pulmonary edema in 96% of cases (32). The reason for high mortality in T2DM patients is combination of several factors. These are atherosclerotic lesions of the distal and proximal parts of the coronary arteries, "metabolic ischemia" reducing contractility of the remaining viable myocardium (14, 33).

2) Perinecrotic or peri-infarction ischemic area that reduces myocardial contractile function under coronary hypoperfusion. The bigger the area, the smaller the cardiac output. In this case, the term "stunned" or "hibernating" (sleeping, inactive) myocardium is used. It should be noted that hyperglycemia increases synthesis of end-stage glycation products and their precursors, thus, in turn, changing the structure of blood proteins and extracellular matrix. The levels of all previous intermediate products of glycolysis are elevated and alternative pathways are activated: glyceraldehyde 3-phosphate, glycerol and methylglyoxal come in the pathways of protein kinase C and final

glycation products; fructose 6-phosphate – in hexosamine pathway; and glucose – in the polyol pathway. All these pathological pathways of glucose and its metabolites utilization are responsible for development of diabetic complications, lesions of nerve tissue and vascular wall (neuropathy and angiopathy) (34, 35). One of the mechanisms determining the significance of T2DM as a risk factor for ALVF is damaging effect of hyperglycemia on the cellular function and metabolism, particularly endothelial cells and cardiomyocytes, resulting in so-called "glucose toxicity" with inevitable apoptosis (35). Thus, it is logical to assume that the presence and severity of "metabolic ischemia" associated with poorly compensated or newly diagnosed T2DM will increase the area of hibernating myocardium and reduce myocardial contractility in patients with impaired CM.

3) Intact myocardium area, when the contractile function will depend on the mass of surviving heart muscle, condition of the intact myocardium (severity of atherosclerotic cardiosclerosis, presence and size of postinfarction scars), adequacy of coronary blood supply to growing needs of the myocardium. It is known that the post-infarction cardiosclerosis in T2DM patients is more common than in patients with normal CM (36). According to the morphological studies in patients who died suddenly, atherosclerotic plaques in T2DM patients contain more adipose cells, macrophages and T-lymphocytes compared to those without T2DM (37). Even in asymptomatic T2DM patients, > 50% stenosis is simultaneously observed in several arteries (36, 38). In addition to typical atherosclerotic angiopathy, sclerotic damage of the arterial media develops in T2DM patients and manifests as medianecrosis, mediasclerosis, and mediacalcinosis. This macro-angiopathy is characterized with lesions located in the middle layer of large arteries and accumulation of calcium salts, its thickening and sclerosis, as well as combination with other manifestations of diabetic macro-and micro-angiopathy and neuropathy (39, 40). Eventually, the artery is calcified, it becomes rigid, loses its ability to contract and dilate; as a result, adaptive resources are sharply reduced and calcification of small arteries blocks blood circulation through the collaterals (40, 41). Thus, the myocardium not directly affected by the infarction is intact only relatively (42).

Diabetes contributes to a marked and rapid reduction of the myocardial contractile function. Heart failure develops in T2DM patients not only in connection with coronary atherosclerosis, but also due to specific myocardial damage, so-called "diabetic cardiomyopathy". Here, myocardial microvascular damage plays a great role and leads to dramatic decrease in coronary reserve and generalized reduction of myocardial contractility.

Management of AMI patients with ALVF is well-described in the current guidelines and publications, but ALVF incidence and prognosis in T2DM patients are significantly worse, new approaches to treatment of AMI in T2DM patients are required. On Day 1, in T2DM patients with AMI the infarct-related coronary artery should be revascularized mechanically and, if it's impossible within the first 6 hours after the onset, the thrombolytic therapy should be administered (28).

Percutaneous coronary intervention (PCI) is recommended in T2DM patients with concomitant platelet glycoprotein IIb/IIIa inhibitors. In case of stenting in T2DM patients during PCI, it is preferable to use a drug-eluting stent. Mechanical reperfusion using primary PCI is considered as a method of choice in revascularization of T2DM patients during the acute phase of ST-elevation MI. It is currently proven that primary PCI in T2DM patients with AMI provides better survival rate than thrombolytic therapy (43). Timely PCI does not exclude optimal medical therapy: to improve the results of reperfusion therapy and prevent re-thrombosis, concomitant antithrombotic therapy including direct anticoagulants (heparin, enoxaparin) (44), fondaparinux (45), and antiplatelet drugs (aspirin, ticagrelor, prasugrel, clopidogrel) is administered (46, 47).

ALVF management is based on oxygen, diuretics, and vasodilators. Opiates and inotropic agents are used most selectively, and artificial circulation is required in rare cases only (48).

Shortness of breath is the first sign of developing pulmonary edema. Oxygen inhalation under positive pressure increases the intraalveolar pressure and prevents transudation of fluid from the alveolar capillaries, limiting venous return to the thorax (49). Oxygen is indicated for hypoxemia ($SpO_2 < 90\%$), which is associated with increased risk of sudden death. Oxygen cannot be used regularly in patients without hypoxia, as it causes vasoconstriction and reduces cardiac output (50).

In the majority of patients with dyspnea caused by ALVF, symptoms quickly improve

with intravenous loop diuretics as a result of immediate dilation of the veins and subsequent removal of fluid from the vessels. The optimal dose and route of administration (bolus or continuous infusion) are not determined. The recent prospective, randomized clinical study compared 12-hour bolus and continuous infusion. Low dose (equal to existing oral dose) was compared with higher dose (2.5-fold oral dose). No differences in assessment of signs and changes in serum creatinine were observed. However, compared with a low-dose strategy, the higher doses therapy was associated with a more pronounced improvement in patients' status (including dyspnea), but at the expense of a more pronounced transient deterioration of renal function (50, 51).

Opiates may be useful in ALVF patients, because they reduce anxiety and improve distress related to dyspnea. Painless AMI is often described in the cardiology handbooks and occurs in 10–20% of all AMI (51, 52); however, it is not the same as an asymptomatic AMI. In clinical practice, AMI patients are admitted to coronary ICUs (intensive care units) with complaints of pain behind the breastbone or in the left half of the chest, choking, or combination of these complaints. Feeling of shortness of breath in T2DM patients often comes to the forefront, so it is recommended to consider dyspnea on exertion as an angina equivalent; choking, due to which the patients are admitted to coronary ICUs, is often accompanied by increased levels of cardiac enzymes and is a clinical sign of AMI (5, 11, 53). In this case, it is not required to relieve the pain syndrome, however opiates reduce sympathetic conduct and dilate the veins, thus reducing the preload. The side effects of opiates are nausea and depression of the respiratory activity, which potentially increases the need for invasive lung ventilation (54). Vasodilators, such as nitroglycerin, reduce preload and afterload via increasing LV stroke volume. However, there is no reliable evidence that they relieve dyspnea or improve other clinical outcomes (54, 55). Possibly, vasodilators are mostly indicated for hypertensive patients. They should be avoided in patients with systolic BP <110 mm Hg. Sharp BP fall should be also avoided, as hypotension is associated with high mortality in patients with ALVF. Vasodilators in patients with significant mitral or aortic stenosis are contraindicated, because they decrease BP due to inability to increase cardiac output in response to decreased TPR and increase the lung congestion caused by reflex increase in sympathetic tone and elevated pressure in the left atrium (56). In accordance with the American College of Cardiology/American Heart Association (ACC/AHA) guidelines (57), intravenous infusion of nitroglycerin is indicated within the first 24–48 hours after pain onset in case of anterior *ST*-elevation AMI, persisting myocardial ischemia, heart failure, or hypertension. In case of systolic BP < 90 mm Hg, bradycardia (heart rate (HR) <50 beats per minute), or AMI of the right ventricle, nitroglycerin is contraindicated. In case of inferior AMI, nitrates are also contraindicated, as the pathological process may extend to the right ventricle (58). Beta-adrenoblockers are recommended for all AMI patients in case of adequate blood pressure and heart rate (47). In case of severe heart failure and cardiogenic shock (mean BP <65 mm Hg, pulmonary artery wedge pressure >18 mm Hg, cardiac index <2.2 l/min/m^2), beta-adrenoblockers are contraindicated, as they can deteriorate myocardial contractile function (59, 60). Daily dose of beta-adrenoblockers is individual and determined by the target HR level of 50–60 bpm (57, 60). If not contraindicated, beta-adrenoblockers are preferable as initial therapy, as they are particularly effective in reduction of mortality and incidence of re-MIs in T2DM patients. If there are no obvious contraindications, oral beta-adrenoblockers are recommended for all T2DM patients with ACS (level of evidence A) (4, 60). The course of T2DM in patients receiving insulin or oral glucose-lowering drugs can be complicated with hypoglycemic conditions. Non-selective beta-adrenoblockers can prolong and mask the neurovegetative symptoms of hypoglycemia. That's why selective beta-adrenoblockers are the agents of first choice in ACS with T2DM; their impact on neurovegetative signs is significantly less pronounced compared to non-selective beta-adrenoblockers. Currently, there is an evidence that carvedilol – non-selective beta-adrenoblocker possessing alpha1-adrenoceptor blocking activity – is particularly safe in terms of effects on neurovegetative manifestations in hypoglycemic conditions (57, 60). Carvedilol is able to reduce insulin resistance, therefore its use in T2DM patients especially in combination with chronic heart failure (CHF) has advantages in comparison with other beta-adrenoblockers (level of evidence B) (4).

Selective beta-1-adrenoblockers (metoprolol, bisoprolol) are useful in patients with

reduced heart rhythm variability, often detected in T2DM patients as a sign of DACN (61). It is manifested as rigid pulse with high heart rate requiring higher doses of beta-adrenoblockers compared to non-T2DM patients (60). Long-acting agents (24 hours) with better cardio-selective action are preferable, i.e. bisoprolol. Beta-adrenoblockers with peripheral vaso-dilation activity (nebivolol, carvedilol) were found to have a positive effect on concomitant hypertriglyceridemia (level of evidence C). The vast majority of T2DM patients have clinical manifestations of CHF (62, 63), thus bisoprolol and carvedilol are the first-line drugs (level of evidence A) (60, 64). Additional properties of nebivolol, namely modulation of the endogenous synthesis of nitric oxide and reduction of oxidative stress severity, improve endothelial function, thus increasing the clinical efficacy and ability to improve prognosis in patients with heart failure and T2DM. The clinical status of patients improves with nebivolol (65). Due to reduction in the sympathetic nervous system activity, absence of intrinsic sympathomimetic activity and realization its effects through activation of endothelial nitric oxide (NO) system, nebivolol reduces post-ACS mortality in T2DM patients which is confirmed by several large studies (level of evidence A) (66).

Angiotensin-converting-enzyme inhibitors (ACEIs) are widely used within the first day after AMI (57, 67). They are particularly effective in patients with large myocardial necrosis, reduced LV function and ejection fraction (EF) <40%, symptomatic heart failure and T2DM (68). In T2DM patients, coronary lesions often manifest as clinical heart failure combined with low EF and in case of decompensation or without pharmacological correction of affected CM – with a “metabolic ischemia” of the myocardium. Given that many T2DM patients with ST-elevation AMI have unstable hemodynamics within the first hours, it is recommended to start treatment with low-dose ACE inhibitors (57). If systolic BP is < 100 mm Hg, the agents should be temporarily cancelled, and after BP recovery, the treatment may be restarted with the reduced dose. During treatment, creatinine and potassium levels in the blood serum should be monitored, especially in case of impaired renal function (60), which is often found in T2DM patients – diabetic nephropathy. The MDRD study showed that if glomerular filtration rate (GFR) is < 25 ml/min, ACE inhibitors are dangerous because of their hypotensive action with renal failure worsening. Meanwhile, ACEI benefits overweigh the risk of complications in patients with GFR > 25 ml/min (69). Analyzing the literature and programs of All-Russian and international cardiology conferences, forums and meetings over 2011–2013, we found only a few publications and reports dedicated to the issues of pathogenesis, epidemiology and treatment strategies in T2DM patients with AMI complicated with ALVF. Thus, once again we need to return to the real facts of today: namely, approximately 30% of AMI patients admitted to the hospitals have impaired CM; ALVF-complicated AMIs are 3 times as often in T2DM patients; mortality in T2DM patients with AMI is 2 times higher compared with patients with normal CM. The investigation of mortality causes in T2DM patients with AMI is of primary importance for justification of the program for CVD prevention and mortality reduction in this large population.

References

1. Healthcare in Russia. Federal Service of State Statistics, 2011, 2–8. (In Russian)
2. Mayorov A. Yu. IDF Congress – 2011: new algorithm for treatment of patients with type 2 DM is presented. Effektivnaya farmakoterapia (Effective pharmacotherapy), 2012, 1, 2. (in Russian)
3. Dedov I.I. Innovational technologies in treatment and prevention of the diabetes mellitus and its complications. Sakharniy diabet (Diabetes mellitus), 2013, 3, 2–10. (In Russian)
4. All-Russian guidelines for treatment of ACS without consistent ST elevation on the ECG. 2006. p. 184–193, 196–201, 211–213. (In Russian)
5. Syrkin A. L., Novikova N.A., Terekhin S.A. Acute coronary syndrome. M., MIA, 2003, 2010, 458. (In Russian)
6. Shakhnovich R.M. Acute coronary syndrome with ST elevation. M, GEOTAR – Media, 2010, 17–18. (In Russian)
7. Miettinen H., Lehto S., Salomaa V. et al. Impact of diabetes on mortality after the first myocardial infarction. The FINMONICA Myocardial Infarction Register Study Group Diabetes Care, 1998, 21, 1, 69–75.
8. Tu J.V. A Cluster Randomized Trial of Public Report Cards for Improving the Quality of Cardiac Care: Results from the Canadian Cardiovascular Outcomes Research Team's (CCORT) Enhanced Feedback for Effective Cardiac Treatment (EFFECT). AHA Scientific Sessions. 14–18 ноября 2009, 81–89.
9. Brogan G.X. Jr., Peterson E.D., Mulgund J. et al. Treatment disparities in the care of patients with and without diabetes presenting with non-*ST*-segment elevation acute coronary syndromes. Diabet. Care. 2006, 29, 1, 9–14.
10. Haffner S.M., Lehto S., Rönnemaa T. et al. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N. Engl. J. Med. 1998, 339, 4, 229–234.
11. Kakorin S.V. Complications and mortality related to acute myocardial infarction in patients with type 2 diabetes melli-

tus. Kardiovaskularnaya terapia I profilaktika (Cardiovascular therapy and prevention), 2012, . 11 (June, special edition), 48. (in Russian)
12. Gray A., Goodacre S., Newby D.E. et al. Noninvasive ventilation in acute cardiogenic pulmonary edema. N. Engl. J. Med. 2008, 359, 142–151.
13. Kakorin S.V., Shashkova L.S., Mkrtumyan A.M. Acute coronary syndrome in patients with impaired carbohydrate metabolism. Serdtse (Heart), 2012, 11, 1 (63), 8–12. (In Russian)
14. Barzilay J., Kronmal R., Bittner V. et al. Coronary artery disease and coronary artery bypass grafting in diabetic patients aged >65 years (Report from the coronary artery surgery study (CASS) registry). Am. J. Cardiol., 1994, 74, 334–339.
15. Dedov I.I., Aleksandrov An.A. Problems of acute myocardial infarction in patients with diabetes mellitus: Munich echo. Sakharniy diabet (Diabetes mellitus), 2008.1, 4–10. (In Russian)
16. Kakorin S.V., Karamyshev D.V., Ilina T.O. Comparative analysis of complications in patients with type 2 diabetes mellitus and normal carbohydrate metabolism who died from acute myocardial infarction. Proceedings of the IV All-Russian meeting "Emergency Cardiology2011". Moscow, 24–25.11.2011. p. 62. (In Russian)
17. Mallinson T. Myocardial Infarction. Focus on First Aid, 2010, 15, 3–6.
18. Valensi P., Paries J., BrulportCerisier V. Predictive Value of Silent Myocardial Ischemia for Cardiac Events in Diabetic Patients. Influence of age in a French multicenter study. Diabet. Care. 2005, 28 (11), 2722–2727.
19. Sima A.A., Thomas P.K., Ishii D., Vinik A. Diabetic neuropathies. Diabetologia. 1997, 40 (3), 74–77.
20. Shaw J.E., Zimmet P.Z., Gries F.A. et al. Epidemiology of diabetic neuropathy. Textbook of diabetic neuropathy. Stuttgart, New Jork, 2003, 64–82.
21. Hamm C.W., Bassand J.P., Agewall S. et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent STsegment elevation The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent STsegment elevation of the European Society of Cardiology (ESC). Eur. Heart J., 2011, 10, 21–27.
22. Hess O., Karroll J. Clinical assesment of heart failure. Pulmonary oedema. In: Braunvald Heart disease 7 ed. P. Libby, R. Bonow, D. Mann, D. Zipes (eds), 2008, 561 p.
23. Ablina K.N., Kakorin S.V., Averkova I.A. Pulmonary edema in patients with coronary heart disease and impaired carbohydrate metabolism. Proceedings of the 19th Russian National Congress "Human and Drugs". Moscow, April 2327, 2012, 11. (In Russian)
24. Svet A.V., Kakorin S.V., Mkrtumyan A.M. Organization of medical care for patients with type 2 diabetes mellitus and acute coronary syndrome. 6th All-Russian Congress of Endocrinologists. Moscow, May 2731, 2012. The book of abstracts, 205206. (In Russian)
25. Shakhnovich R.M. Acute coronary syndrome with ST elevation. Moscow, GEOTAR – Media, 2010, 221–234. (In Russian)
26. Ehrlich A.D., Gratsianskiy N.A. RECORD registry participants. Acute coronary syndrome in patients with diabetes mellitus. RECORD registry data. Kardiologia (Cardiology), 2011, 11, 16–21. (In Russian)
27. Krugliy L.B., Kakorin S.V., Bochkov P.A. Distribution by gender of patients with impaired carbohydrate metabolism suffering from myocardial infarction and unstable angina. Proceedings of the 19th Russian National Congress "Human and Drugs". M., April 23–27, 2012, 126. (In Russian)
28. Rentrop K.P. Thrombi in acute coronary syndromes: revisited and revised. Circulation. 2000, 101 (13), 1619–1626.
29. O'Connor R.E., Brady W., Brooks S.C. et al. American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Part 10: acute coronary syndromes. Circulation. 2010, 122, 18 (3), 787–817.
30. Buziashvili Yu.I., Asymbekova E.U., Matskeplishvili S.T. Cardiointerventional treatment of patients with type 2 diabetes mellitus and CHD. Sakharniy diabet (Diabetes mellitus), 2008, 1 (38), 35–39. (In Russian)
31. Kakorin S.V., Karamyshev D.V., Ilina T.O. 24-hour mortality from acute myocardial infarction in patients with type 2 diabetes mellitus. Proceedings of the 4th All-Russian Meeting "Emergency cardiology2011". M., November 24–25, 2012, 37. (In Russian)
32. Kakorin S.V., Karamyshev D.V. Cardiogenic shock and pulmonary oedema associated with fatal myocardial infarction in patients with type 2 diabetes mellitus and normal carbohydrate metabolism. Proceedings of the 5th All-Russian Forum "Emergency Cardiology Issues – 2012". M., November 2829, 2012, p. 12. (In Russian)
33. Valensi P., Paries J., BrulportCerisier V. Predictive Value of Silent Myocardial Ischemia for Cardiac Events in Diabetic Patients. Influence of age in a French multicenter study. Diabet. Care. 2005, 28 (11), 2722–2727.
34. Подачина С.В. От классической терапии диабетической нейропатии к решению проблемы гипергликемической памяти. Эффективная фармакотерапия. Эндокринология. 2012, 1, 48–52.
35. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism. Diabetes. 2005, 54 (5), 1615–1625.
36. Dandona P., Chaudhuri A., Ghanim H. Acute Myocardial Infarction, Hyperglycemia, and Insulin. J. Am. Coll. Cardiol. 2009, 53, 1437–1439.
37. Kakorin S.V., Karamyshev D.V., Ilyina T.O. Overdiagnosis of postinfarction cardiosclerosis in patients with type 2 diabetes mellitus and normal carbohydrate metabolism. 6th All-Russian Meeting "Emergency cardiology2011". Abstracts. Moscow, November 2425, 2011. p. 36. (In Russian)
38. Stone G.W., White H.D., Ohman E.M. et al. Acute Catheterization and Urgent Intervention Triage strategy (ACUITY) trial investigators. Bivalirudin in patients with acute coronary syndromes undergoing percutaneous coronary intervention: a subgroup analysis from the Acute Catheterization and Urgent Intervention Triage strategy (ACUITY) trial. Lancet. 2007, 369, 9565, 907–919.
39. Gurevich M.A. Features of pathogenesis and treatment of coronary heart disease, heart failure and arterial hypertension in diabetic patients. Klinicheskaya meditsina (Clinical medicine), 2005, 1, 4–9. (In Russian)
40. Levina L.I., Shapovalova A.B. Diabetes mellitus and coronary heart disease. Vracheb. Vedomosti (Physician's journal), 2005, 3, 33–37. (In Russian)

41. Antsiferov M.B., Staroverova D.N. Methods of diagnosis and treatment of diabetic macroangiopathy. Rossiysky meditsinsky journal (Russian Medical Journal), 2003, 11 (No 27), 1–7. (In Russian)
42. Favaro E., Miceli I., Bussolati B., SchimittNey M. Hyperglycemia Induces Apoptosis of Human Pancreatic Islet Endothelial Cells. Am. J. Pathol. 2008, 173 (2), 442–450.
43. Coronary heart disease and diabetes mellitus: algorithm for diagnosis, prevention and treatment. The Ministry of Healthcare and Social Development of the Russian Federation Federal Agency for Healthcare and Social Development of Federal State Institution Scientific Center of Endocrinology the Rosmedtechnologies, 2007. (In Russian)
44. Antman E.M., Morrow D.A., McCabe C.H. et al.; ExTRACT-TIMI 25 Investigators. Enoxaparin versus unfractionated heparin with fibrinolysis for STelevation myocardial infarction. N. Engl. J. Med. 2006, 354, 1477–1488.
45. Mehta S.R., Boden W.E., Eikelboom J.W. et al. OASIS 5 and 6 Investigators. Antithrombotic therapy with fondaparinux in relation to interventional management strategy in patients with *ST* and non-ST-segment elevation acute coronary syndromes: an individual patientlevel combined analysis of the Fifth and Sixth Organization to Assess Strategies in Ischemic Syndromes (OASIS 5 and 6) randomized trials. Circulation. 2008. 118 (20), 2038–2046.
46. Cayla G., Silvain J., O'Connor S.A. et al. Current antiplatelet options for NSTEACS patients. QJM. 2012, 72–76.
47. Kessler C., Thomas K., Kao J. Antiplatelet therapy for secondary prevention of acute coronary syndrome, transient ischemic attack, and noncardioembolic stroke in an era of cost containment. J. Investig. Med. 2012, 60 (5), 792–800.
48. The ESC guidelines on diagnosis and treatment of acute and chronic heart failure – 2012 Rossiyskiy kardiologicheskiy zhurnal (Russian journal of cardiology), 2012, 4 (102), Appendix 3, 44–46. (In Russian)
49. Malyshev V.D., Vedenina I.V., Omarov Kh.T. et al. Intensive therapy. Moscow. Medicine, 2002, p.217–219. (In Russian)
50. Park J.H., Balmain S., Berry C. et al. Potentially detrimental cardiovascular effects of oxygen in patients with chronic left ventricular systolic dysfunction. Heart. 2010, 96, 533–538.
51. Rosenberg J., Gustafsson F., Galatius S., Hildebrandt P.R. Combination therapy with metolazone and loop diuretics in outpatients with refractory heart failure: an observational study and review of the literature. Cardiovasc. Drugs. Ther. 2005, 19, 301–306.
52. Silva J.A., Ramee S.R., White C.J. et al. Primary stenting in acute myocardial infarction: influence of diabetes mellitus in angiographic results and clinical outcome. Am. Heart J. 1999, 138, 446–455.
53. Oganov R.G., Fomina I.G. Heart diseases. Guidelines for physicians. Moscow, Litterra, 2006, p. 1344. (In Russian)
54. The ESC guidelines on diagnosis and treatment of acute and chronic heart failure - 2012 Rossiyskiy kardiologicheskiy zhurnal (Russian journal of cardiology). 2012, 4 (102), Appendix 3, 45. (In Russian)
55. Cotter G., Metzkor E., Kaluski E. et al. Randomised trial of highdose isosorbide dinitrate plus lowdose furosemide versus highdose furosemide plus lowdose isosorbide dinitrate in severe pulmonary oedema. Lancet. 1998, 351 (9100), 389–393.
56. Romanenko V.V., Romanenko Z.V. Chronic rheumatic heart diseases: primary and secondary prevention, tactics of management and treatment. Meditsinskie Novosti (Medical News), 2009, 9, 32–34. (in Russian)
57. Antman E.M., Hand M., Armstrong P.W. et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With STElevation Myocardial Infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: developed in collaboration With the Canadian Cardiovascular Society endorsed by the American Academy of Family Physicians: 2007 Writing Group to Review New Evidence and Update the ACC/AHA 2004 Guidelines for the Management of Patients With STElevation Myocardial Infarction, Writing on Behalf of the 2004 Writing Committee // Circulation. 2008, 117 (2), 296–329.
58. Bauer T., Zahn R. Modern treatment in acute coronary syndrome, Dtsch. Med. Wochenschr. 2012, 137 (14), 722–725.
59. Griffin B., Topol E. Cardiology. Practice. Moscow, 2008, p. 100. (In Russian)
60. Anderson J.L., Adams C.D., Antman E.M. et al.; American College of Cardiology; American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-STElevation Myocardial Infarction); American College of Emergency Physicians; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons; American Association of Cardiovascular and Pulmonary Rehabilitation; Society for Academic Emergency Medicine. ACC/AHA 2007 guidelines for the management of patients with unstable angina/nonST-Elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/NonSTElevation Myocardial Infarction) developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. J. Am. Coll. Cardiol. 2007, 50 (7), 1–157.
61. Valensi P., Paries J., BrulportCerisier V. Predictive Value of Silent Myocardial Ischemia for Cardiac Events in Diabetic Patients. Influence of age in a French multicenter study. Diabet. Care. 2005, 28 (11), 2722–2727.
62. Haas S.J., Vos T., Gilbert R.E., Krum H. Are betablockers as efficacious in patients with diabetes mellitus as in patients without diabetes mellitus who have chronic heart failure? A metaanalysis of largescale clinical trials. Am. Heart J. 2003, 146 (5), 848–853.
63. Averkova I.A., Kakorin S.V., Ablina K.N. Chronic heart failure in patients with type 2 diabetes mellitus and acute coronary syndrome. Proceedings of the 19th Russian National Congress "Human and Drugs". M., April 23–27, 2012, 4–6. (In Russian)
64. Averkov O.V., Modern guidelines for diagnosis and treatment of ACS with ST elevation. Russian National Congress of Cardiologists "Integration of knowledge in cardiology". Moscow, October 3–5, 2012, 30. (In Russian)

65. Latfullin I.A., Ishmurzin G.P. Autonomic nervous system function and effects of beta-adrenoblockers on heart rhythm variability in patients with myocardial infarction. Klin. Med. (Mosk). 2002, 80 (9), 22–27.
66. Dedov I.I., Aleksandrov A.A. Risk factors for coronary heart disease in patients with type 2 diabetes mellitus: role of hypersympathicotonia and possibilities of its correction. Quality of life. Medicine. Diabetes mellitus. 2003, 1, 16–23. (In Russian)
67. Diagnosis and Treatment of Patients with Acute Myocardial Infarction with ST-elevation on the ECG: Russian Guidelines. All-Russian Scientific Society of Cardiology. M., 2007 (In Russian)
68. Demidova T.Yu., Kosykh S.A. The role and place of angiotensin receptor blockers in correction of metabolic syndrome components in patients with type 2 diabetes mellitus. Rossiysky meditsinsky journal (Russian medical journal), 2005, 6, Endocrinology, 334–339. (In Russian)
69. Dedov I.I., Shestakova M.V. Diabetes mellitus: acute and chronic complications. Medical Information Agency. Moscow, 2011, 294–300. (In Russian)

Complications After Stenting of the Aortic Arch Arteries (Review)

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Stenting of the aortic arch arteries is an effective option for primary prevention of ischemic stroke. However, the complications may develop during intervention or after it as for any other surgical intervention. The article reviews various complications related to stenting of the aortic arch arteries, methods of their prevention, diagnosis, and treatment.

Key words: *complications of stenting of the aortic arch arteries; hypotension, bradycardia; cerebral arterial spasm; subarachnoid hemorrhage; brain hyperperfusion syndrome; distal embolism; contrast-induced encephalopathy, carotid artery rupture.*

One of the important neurological problems is the treatment of patients with cerebral vascular accident, primarily due to high incidence of such a severe disease as ischemic stroke. Mortality from cerebral vascular accident (CVA) in economically developed countries ranges from 12 to 29% second only to heart diseases and malignancies (1, 2). Among the main causes of ischemic stroke, there are extracranial atherosclerotic lesions of the brachycephalic arteries (BCAs) and intracranial atherosclerosis accounting for up to 70% and 8–9%, respectively (3, 4). The surgical treatment options for BCAs atherosclerosis are proved to reduce significantly the risk of CVA and improve prognosis in these patients (4–8). The endovascular treatment option for BCAs atherosclerosis – stenting – has been increasingly used. The outcomes of these interventions are currently non-inferior to carotid endarterectomy (CE) and superior significantly to open procedures in case of lesions of the vertebral arteries, intracranial parts of BCAs, and before CABG (4, 7, 8).

To improve the results of endovascular treatment of BCAs stenotic lesions, the possible complications and measures of their prevention should be analyzed. Peri-operative and post-operative complications after BCAs stenting may be mild and severe. The mild complications include: carotid arterial spasm, hypotension-bradycardia, and TIA; the severe ones are: distal embolism, intracranial hemorrhage, hyperperfusion syndrome, arterial dissection, carotid artery rupture, acute in-stent thrombosis, contrast-induced reaction (9).

Mild complications. 1. Intra-operative hypotension and bradycardia. Bradycardia or asystole often manifests as physiological reaction to balloon dilatation in the carotid body area (carotid artery bifurcation) (10). Such hemodynamic instability can be prevented by temporary pacing or administration of atropine 0.5–1 mg. Higher doses of atropine should not be administered to elderly subjects, as it may make difficult the assessment of their neurological condition and cause exacerbation of cardiac pathology. For early detection of complications and appropriate measures to be taken, it is reasonable to closely monitor hemodynamics in all patients during the intervention and within the first hours after it. It should be noted that in case of clinical signs, other possible causes of hypotension/bradycardia must be excluded: acute bleeding, heart diseases, bleeding from the vascular access. Patient's hemodynamics should be immediately stabilized in the following cases: occluded contralateral carotid artery, severe vertebrobasilar stenosis, significant stenoses of the intracranial BCAs, progression of neurological symptoms related to distal embolism. In practice, hypotension is well managed by intravenous hydration and/or low doses of vasopressors (11).

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2. Prolonged postoperative hypotension occurs after 4–11% of carotid stentings (CSs) (12). Usually, it is not associated with any adverse effects during hospitalization. However, some studies demonstrated adverse consequences associated with this clinical event (13). Perhaps, hypotension is more pronounced in patients with hypovolemia or heart disease progression. The independent predictors of prolonged hypotension after BCAs stenting are: age, transient hypotension during balloon dilatation, use of self-expanding stents, stenting of calcified stenosis (9). The prolonged hypotension after CS is usually caused by sinocarotid reflex. Stimulation of the carotid body leads to reflex hypotension and bradycardia. The correctness of this judgment can be confirmed by the fact that this complication does not develop when intracranial parts of BCAs and vertebral arteries are stented. To prevent the difficulties associated with this situation, it is necessary to closely monitor BP and HR during and after intervention. Usually, this complication is well managed with intravenous hydration and/or low doses of vasopressors (9, 14). However, if hypotension is observed on Day 1 after intervention, complication at the femoral artery puncture site should be considered.

3. Arterial spasm. Reflex narrowing of the internal carotid artery (ICA) or vertebral artery (VA) after the filter placement or deep arterial cannulation with guiding catheter is a complication that often resolves spontaneously after device withdrawal from the artery (15). Caution during intervention and application of guiding catheter with soft tip minimize the possibility of arterial spasm. This complication may be particularly dangerous in case of significant atherosclerotic lesions of the contralateral arteries or incomplete circle of Willis. Intra-arterial nitroglycerin 100–400 μg or calcium antagonists through the guiding catheter usually resolve spasm quickly (10, 15).

Severe complications. 1. Subarachnoid hemorrhage. This complication, according to various data, occurs approximately in 0.3% of cases (9, 10). Clinical sign of this severe complication is loss of consciousness preceded by severe headache in the absence of intracranial artery occlusion. The angiographic signs may be as follows: generalized vascular spasm or extravasation of contrast medium. The diagnostics option is an emergency computed tomography (CT). The probable causes of spontaneous intracerebral hemorrhage are: intensive anticoagulant therapy, hypertension, arterial aneurysms, prior ischemic stroke (>3 weeks earlier), injuries of intracranial arteries caused by guidewires or other devices (9, 10).

2. Brain hyperperfusion syndrome. It is reported in 0.3–2.7% of cases (16–18). The clinical manifestations are prolonged headaches, nausea, vomiting, increased blood pressure, seizures, loss of consciousness, and intracranial bleeding. The mortality rate related to intracranial hemorrhage with hyperperfusion syndrome is 36-63%. The factors triggering this syndrome are: critical carotid artery stenosis, insufficient collateral blood flow, occluded contralateral BCA, recanalization of occluded BCA, simultaneous stenting of two or more BCAs. The pathophysiological mechanisms include long-term hypoperfusion and impaired autoregulation of microcirculation. Perfusion pressure increases after revascularization, however, microvasculature is not able to capture the increased blood volume and the clinical signs develop. The hyperperfusion syndrome is diagnosed on the basis of clinical data and results of transcranial Doppler (TCD). The measures to prevent this dangerous complication include early diagnosis and BP monitoring during intervention and after it (7, 16, 18, 19).

3. Distal embolism. Symptomatic distal embolism is the most common and serious complication of BCAs stenting and caused by thrombotic or atherogenic masses dislocated in the distal segment. Prior to era of the distal embolic protection devices, the incidence of ischemic strokes due to this complication reached up to 22%. Owing to widespread introduction of the embolic protection devices into clinical practice, these complications are currently 4 times less common (9, 11, 13, 20). However, it is difficult to use the embolic protection devices for stenting of the intracranial parts of the BCAs and V3–V5 segments of the Vas; this, in turn, may increase the risk of this complication. The risk factors for distal embolism associated with BCAs stenting include: soft atherosclerotic plaque or fresh blood clot, medical therapy (previous inadequate treatment with two antiplatelet agents, resistance to clopidogrel, inadequate heparin therapy during intervention), technique of stenting (intervention without embolic protection system, sudden movement of stent or balloon catheter, “forced” pushing the stent through a calcified atherosclerotic plaque, multiple attempts to guide the tools through a

Types, prevention measures, diagnostics and treatment of complications after stenting of the aortic arch arteries

Complication	Clinical presentation	Diagnostics	Prevention measures	Treatment
Intra-operative hypotension/ brady-cardia	Intra-operative bradycardia, asystole, and hypotension.	1. ECG. 2. BP monitoring.	Temporal pacing and/or administration of atropine.	1. Administration of atropine. 2. Vasopressor support and/or infusion therapy.
Postoperative hypotension	Bradycardia, asystole, and hypotension.	1. ECG. 2.BP monitoring. 3. USDI of the puncture site. 4. Abdominal US.	1. Adjustment of antihypertensive therapy. 2. Use of arterial closure devices.	1. Adjustment of the antihypertensive therapy. 2. Adjustment of the hypovolemia. 3. Suturing of the femoral artery (in case of bleeding).
Arterial spasm	1. Angiographic signs of local vasospasm. 2. Progression of neurological deficits specific for arterial intervention area.	1. CA. 2. TCD.	Selective administration of calcium antagonists.	Selective administration of calcium antagonists.
Intra-operative SAH	1. Severe headache. 2. Progression of cerebral symptoms (depression or loss of consciousness, severe headache). 3. No occlusion of intracranial arteries. 4. Generalized vasospasm. 5. Signs of extravasation of contrast medium.	1. CA. 2. Brain CT	1. Continuous monitoring of the guidewire or distal protection system to prevent arterial perforation. 2. Intra-operative BP monitoring. 3. Control over patient's hemostatis.	1. Administration of protamine sulfate. 2. Attempt to occlude the arterial defect (in case of intra-operative hemor-rhage). 3. Hematoma removal (if necessary).
Post-operative SAH	1. Progression of cerebral symptoms (depression or loss of consciousness, severe headache). 2. No occlusion of intracranial arteries. 3. Generalized vasospasm.	1. Brain CT. 2. USDI of the stented segment.	1. Intra- and postoperative BP monitoring. 2. Control over patient's hemostatis.	Hematoma removal (if necessary).
Brain hyperperfusion syndrome	1. Prolonged headache. 2. Increased BP. 3. Focal neurological deficit. 3. Nausea. 4. Vomiting. 5. Seizures. 6. Intracranial hemorrhage.	1. TCD. 2. CT brain perfusion. 3. MRI perfusion.	Postoperative BP monitoring.	1. Postoperative management of the patient under controlled hypotension. 2. In case of SAH - hematoma removal (if necessary).

Distal embolism	1. Progression of neurological deficits specific for arterial intervention area. 2. Angiographic signs of thrombotic occlusion of the cerebral arteries.	1. CA.	1. Distal or proximal protection devices. 2. Proper selection of the distal protection system diameter (0.5 mm larger than the diameter of the artery). 3. Control over patient's hemostatis.	1. Thrombus extraction. 2. Platelet glycoprotein IIb/IIIa receptor antagonists (Eptifibatide), if there are signs of thrombosis. 3. Selective thrombolysis. 4. If the clot is impossible to remove – the treatment is according to the standard of care for ischemic stroke.
Arterial dissection	1. Angiographic signs of artery dissection. 2. Possible progression of neurological deficits specific for arterial intervention area.	1. CA. 2. USDI of the stented segment.	1. Proper selection of the diameter of the stent and balloon catheter for dilatation. 2. Careful manipulation of the guiding catheter and distal protection system.	1. Stenting of the dissection area. 2. Platelet glycoprotein IIb/IIIa receptor inhibitors (Eptifibatide), if there are signs of thrombosis.
Arterial rupture in the stenting area	Angiographic signs of extravasation of contrast medium in the stenting area.	1. CA. 2. USDI of the stented segment.	Proper selection of the diameter of the stent and balloon catheter for dilatation.	1. Administration of protamine sulfate. 2. Stenting and use of stent-graft (if desired size exists). 3. Suturing the ruptured artery.
Acute in-stent thrombosis	1. Progression of neurological deficits specific for arterial intervention area. 2. Angiographic and US evidence of thrombotic in-stent occlusion.	1. CA. 2. USDI of the stented segment.	1. Proper selection of the stent diameters. 2. Monitoring the antiplatelet therapy.	1. Balloon angioplasty of the thrombosis area (application of proximal protection systems for prevention of distal embolism). 2. Re-stenting (if necessary). 3. Platelet glycoprotein IIb/IIIa receptor inhibitors (Eptifibatide). 4. Selective thrombolysis (if platelet glycoprotein IIb/IIIa receptor inhibitors could not be used). 5. Mechanical thrombus removal. 6. If impossible to restore a lumen of the artery or in case of significant collateral circulation – the treatment is according to the standard of care for ischemic stroke.
Contrast-induced encephalopathy	1. Progression of neurological deficit. 2. Spontaneous regression in 24 hours.	1. CA (no pathology). 2. Brain CT (no pathology). 3. USDI of the stented segment		Follow-up.

tortuous artery) (9). During intervention it is necessary to evaluate the patient's neurological deficits or, if it is not possible, to monitor cerebral blood flow using TCD (6, 21, 22). If neurological symptoms deteriorate, CA should be performed to localize the emboli and degree of collateral blood flow. When carotid artery (CA) or vertebrobasilar branch is stented, the emboli typically move to the distal parts of ICA and MCA or basilar artery and PCA, respectively. If the emboli are detected, the measures should be taken to recanalize cerebral arteries (thrombus extraction, selective thrombolytic therapy, balloon angioplasty or use of platelet glycoprotein IIb/IIIa receptor antagonists). If these procedures are impossible or inadequate, standard treatment for ischemic stroke is conducted. In parallel, it is necessary to manage hemodynamics and, if the patient is agitated, to perform general anesthesia. It should be considered that the changes in neurological status may also be associated with intracranial hemorrhage, hyperperfusion syndrome, or contrast-induced reaction. If multiplane angiogram demonstrates no sign of distal embolism, a brain CT should be performed to exclude hemorrhage.

4. Arterial dissection. This complication is quite rare, but has serious consequences (9, 23). The detachment of the intimal layer may lead to thrombosis, distal embolism and/or complete occlusion of the artery. The factors increasing the risk of dissection are: BCA tortuosity or "loops", damage caused by tools (guiding catheter, distal embolic protection device, balloon catheter, stent delivery system or stent), aggressive manipulation of tools. This complication may have no clinical signs. To diagnose arterial dissection, angiography should be performed after intervention not only in the interventional area but in the distal and proximal parts of BCA (preferably in two or more projections). Typically, the dissection is easily resolved with stenting, so before performing interventions in the catheterization laboratory, a set of stents and tools to manage this serious complication should be available. If there are signs of thrombosis, it is advisable to use platelet glycoprotein IIb/IIIa receptor antagonists (9, 23, 24).

5. Artery rupture. This complication is rarely reported in the literature. Cremonesi A. et al. reported only one (0.08%) carotid artery rupture in 1150 patients who underwent CA stenting (25). The cause of this complication is the large diameter of balloon-extended stent or balloon catheter for post-dilatation. To prevent this complication, a sufficient set of tools should be available in the cath lab and surgical intervention should be thoroughly prepared (9, 24).

6. Acute in-stent thrombosis. This complication is also very rare (9, 11, 24). It is caused by inadequate antiplatelet therapy, in particular, resistance to clopidogrel, patient's refusal to take medications, or coagulopathy. The risk of in-stent thrombosis is also affected by operative factors, such as selection of the stent with appropriate diameter, adequate blood flow within the stent and dissection of the proximal and distal segments of the artery. If thrombosis occurs during intervention or in the early postoperative period, it is advisable to assess neurological signs and extent of brain lesions, as well as to consider the thrombus extraction and thrombolysis. In case of asymptomatic in-stent thrombosis in the postoperative period, the antiplatelet therapy should be modified and prolonged. Excessive aggressive treatment of asymptomatic acute thrombosis may lead to distal embolism and is not always justified. For treatment of acute symptomatic in-stent thrombosis, it is advisable to take into account the condition of the cerebral arteries and use the proximal protection system and thrombus extractors for removing emboli from the distal BCA, as well as platelet glycoprotein IIb/IIIa receptor antagonists or fibrinolytic agents (9, 11, 23).

7. Contrast-induced encephalopathy. This complication is extremely rare (< 0.1% cases) and usually associated with prolonged procedure and large amount of contrast medium. The patient may develop neurological deficit, although there are no contrast-enhanced defects in BCA and CT provides no evidence of intracranial hemorrhage. The contrast medium is known to not penetrate the blood-brain barrier and the neurological deficit can be explained by distal embolism with particles of contrast medium. Usually, patients completely recover in 24 hours. There is no permanent neurological deficit (9, 26).

Predictors of complications were investigated in numerous studies. For example, Herbert D. et al. investigated predictors of CS complications in 2104 patients with a high risk for CE. The study involved 84 multidisciplinary clinics. 1.3% of patients died during hospitalization: 9 (0.4%) patients from CVA, other died from the puncture site complications or other causes; 25 (1.1%) and 87 (4%) patients had AMI and CVA, respectively. 30-day CVA and neurological

death were reported in 88 (4.2%) patients. The majority (91%) of these events occurred within two weeks after intervention. The main predictors of 30-day CVA and death were as follows: age ⩾66 years, symptomatic stenosis of the ICA, as well as clinic experience. The following predictors of complications were identified using multivariate analysis: age over 70 y.o. (continuous variable), Afro-American race, angiographic visible thrombus in the ICA (in symptomatic patients), IIb/IIIa receptor inhibitor used during intervention, procedural TIA, residual stenosis >30%, intraoperative use of agents to increase systemic blood pressure. After multivariate analysis, only age over 70 y.o. (RR = 1.05; 95% CI: 1.03–1.08; p = 0.001) and CVA within 180 days before CS (RR = 2.56; 95% CI: 1.13–5.79; p = 0.024) were statistically significant (26).

The question on the complication risks in elderly patients is currently controversial. Several large studies demonstrated the increased risk of complications in elderly patients. The objective of the study conducted by R. Zahn et al. was to identify the influence of age on risk of postoperative complications after 1870 CSs. Operation time, duration of in-hospital stay, intraoperative complications, and problems at the puncture site were significantly increased in the group of patients aged from 70 to 79 y.o. and older (5.5 versus 3.2%; RR = 1.79; 95% CI: 1.04–3.06, p = 0.032). Logistic regression analysis showed that age from 70 to 79 y.o. was a strong factor for in-hospital mortality and stroke (p < 0.001), whereas the age group of 80 y.o. and older demonstrated only a trend to increased number of adverse events (p = 0.062) (27).

Stenting results often depend on the type of tools used for intervention. In particular, A. Cremonesi et al. evaluated the results of CS using open- and closed-cell design stents in 1317 patients with symptomatic stenoses of the cervical segment of the ICA. Most interventions were performed using the distal protection devices. 30-day adverse events (CVA, AMI, and death) were observed in 48 (3.6%) patients. 30-day adverse events were reported in 2.2% and 7% of patients who were implanted with closed- and open-cell design stents, respectively (p < 0.0001). The authors conclude that the best results were obtained when the closed-cell design stents (tighter weaving) were used due to tighter pressing of the injured intima, blood clots, and atheromatous masses and, consequently, lower frequency of distal embolism and in-stent thrombosis. The authors consider the tortuosity of the carotid arteries as the main reason for intra-operative technical difficulties (28).

It should be noted that post-CS complications usually lead to severe neurological disorders; therefore, when endovascular treatment of BCA stenoses is planned, the possible complications and ways of their management should be considered. Based on the reviewed literature (1–41), we tried to formulate the algorithms for diagnosis and treatment of post-BCA stenting complications (see Table).

References

1. American Heart Association. Stroke Statistic. Dallas, American Heart Association, 2000.
2. Rosamond W. Heart Disease and Stroke Statistics – 2008 Update. A Report From the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2008, 117, e25–e146.
3. Henkes H., Miloslavski E., Lowens S. et al. Treatment of intracranial atherosclerotic stenoses with balloon dilatation and selfexpanding stent deployment (WingSpan). Neuroradiology. 2005, 47, 222–228.
4. Members F., Tendera M., Aboyans V. et al. EESC Guidelines on the diagnosis and treatment of peripheral artery diseases. Eur. Heart J. 2011, 32, 2851–2906.
5. Kuznetsov A.N., Vinogradov, O.I., Zhabotinskaya M.G. Ischemic stroke. Diagnostics, treatment, prophylactics. (A textbook). M.: B.I., 2009, p. 48. (In Russian)
6. Kucherenko S.S. Clinical safety of open and endovascular interventions on the carotid arteries. Abstract of Dr. Med. Sci. thesis. M., 2012. p. 48. (In Russian)
7. Compter A., Worp H., Schonewille W. et al. VAST: Vertebral Artery Stenting Trial. Protocol for a randomised safety and feasibility trial. Trials. 2008, 9, 65–74.
8. Members F., Tendera M., Aboyans V. et al. EESC Guidelines on the diagnosis and treatment of peripheral artery diseases Uropean. Heart J. 2011, 32, 2851–2906.
9. Castriota F., Cremonesi A., Tavazzi L. Carotid stenting complications. Eur. J. Cardiol. Pract. 2010, 8, 7.
10. Mubarak N., Liu M., Dean L. Incidences and outcomes of prolonged hypotension following carotid artery stenting. J. Am. Coll. Cardiol. 1999, 33, 65.
11. Robert W., Robert H. Interventional neuroradiology Informa. Healthcare USA, Inc. 52 Vanderbilt Avenue New York, 2008, 161–305.
12. Dangas G., Laird J., Satler L. et al. Postprocedural hypotension after carotid artery stent placement: predictors and short and longterm clinical outcomes. Radiology. 2000, 215, 677–683.
13. Ringleb P., Allenberg J., Bruckmann H. et al. 30 day results from the SPACE trial of stentprotected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised noninferiority trial. Lancet. 2006, 368, 1239–1247.
14. Koenigsberg R., Bianco B., Faro S. et al. Textbook of Clinical Neurology. Saunders Elsevier, 2007.
15. Shevchenko Yu.L., Kuznetsov A.N., Kucherenko S.S. et al. Cerebral vasospasm in endovascular interventions on cere-

bral vessels. Vestnik N.I. Pirogova NMHC (Herald of N.I. Pirogov Scientific Medical Center of Surgery), 2010, 5, 4, 2–16. (In Russian)
16. Belyaev A.Yu, Usachev D.Y., Lushkin V.A. et al. Cerebral hyperperfusion syndrome after carotid endarterectomy. Voprosy neurokhirurgii (Problems of Neurosurgery), 2011, 3, 31–38. (In Russian)
17. Pokrovskiy V.A., Dan V.N., Narlyev K.M. et al. The immediate results of carotid endarterectomy in patients with residual signs of stroke. Khirurgiya (Surgery).1993, 5, 16–23. (In Russian)
18. Naylor A., Ruckley C. The postcarotid endarterectomy hyperperfusion syndrome. Eur. J. Vasc. Endovasc. Surg. 1995, 9, 365–367.
19. Chimowitz M., Lynn M., Derdeyn C. et al. Stenting versus aggressive medical therapy for intracranial arterial stenosis. N. Engl. J. Med. 2011, 11, 993–1003.
20. Kuznetsov A.N. Cerebral embolism: past, present, future of the problem. Nevrologichesky journal (Nevrological journal). 2004, 9, 5, 4–11. (In Russian)
21. Gaydar B.V., Semenyutin B.V., Parfenov V.E. Transcranial Doppler ultrasonography in neurosurgery. SPb, Elib publishing house. Saint Petersburg, 2008, 208–221. (In Russian)
22. Kuznetsov A.N. Cardiogenic and arterioarterial cerebral embolism: Etiology, pathogenesis, clinic, diagnostics, treatment, and prevention. Abstract of Dr. Med. Sci. thesis. SPb., 2001, p. 32. (In Russian)
23. Roubin G., Vitek J., Iyer S. et al. Subarachnoidal hemorrhage following carotid stenting with the distalballoon protection. Catheter Cardiovasc. Interv. 2001, 54, 521–523.
24. Bokeria L.A., Alekyan B.G. Guidelines for Xray endovascular surgical treatment of the cardiac and vascular diseases in 3 volumes. Moscow, publishing house of Bakoulev Center for cardiovascular Surgery, 2008, 135–205. (In Russian)
25. Cremonesi A., Setacci C., Manetti R. et al. Carotid angioplasty and stenting: lesion related treatment strategies. EuroIntervention. 2005, 1, 289–295.
26. Herbert D, William A., Stephen R. et al. Predictors of Neurological Events Associated With Carotid Artery Stenting in HighSurgicalRisk Patients: Insights From the Cordis Carotid Stent Collaborative. Circ. Cardiovasc. Interv. 2010, 3, 577–584.
27. Zahn R., Ischinger T., Hochadel M. et al. Carotid artery stenting in octogenarians: results from the ALKK Carotid Artery Stent (CAS) Registry. Eur. Heart J. 2007, 2, 370–375.
28. Cremones A., Grattoni C., Colombo F. et al. The Tailored Approach To CAS. Inssert to Endovasc. Today. 2010, 16, 29–33.
29. Shevchenko Yu.L., Odinak M.M., Mikhaylenko A.A. et al. Cardioembolic stroke. (Textbook). SPb., B.I., 1997, p. 66. (In Russian)
30. Bauer R. Joint study of extracranial arterial occlusion. Progress report of controlled study of longterm survival in patients with and without operation. J.A.M.A. 1969, 208, 509.
31. Berguer R., Flynn L., Kline R. et al. Surgical reconstruction of the extracranial vertebral artery: management and outcome. J. Vasc. Surg. 2000, 31, 9–18.
32. Caplan L., Wityk R., Glass T. et al. New England Medical Center Posterior Circulation registry. Ann. Neurol. 2004, 56, 389–398.
33. Crawford P., West C., Chadwick D. et al. Arteriovenous malformations of the brain: natural history in unoperated patients. J. Neurol. Neurosurg. Psychiatr. 1986, 49, 1–10.
34. Fiorella D., Levy E., Turk A. et al. US multicenter experience with the Wingspan stent system for the treatment of intracranial atheromatous disease: periprocedural results. Stroke. 2007, 38, 881–887.
35. Gupta R., AlAli F., Thomas A. et al. Safety, feasibility, and shortterm followup of drugeluting stent placement in the intracranial and extracranial circulation. Stroke. 2006, 37, 2562–2566.
36. Howard Рю, Helmi L,. Lutsep M. et al. Influence of sex on outcomes of stenting versus endarterectomy: a subgroup analysis of the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). Lancet Neurol. 2011, 10, 530–537.
37. Kjellin I., Boechat M., Vinuela F. et al. Pulmonary emboli following therapeutic embolization of cerebral arteriovenous malformations in children. Pediatr. Radiol. 2000, 30, 279–283.
38. Levy E., Turk A., Albuquerque F. et. al. Wingspan instent restenosis and thrombosis: incidence, clinical presentation, and management. Neurosurgery. 2007, 61, 644–650.
39. Timaran C., Rosero E., Smith S. et al. Trends and outcomes of concurrent carotid evascularization and coronary bypass. J. Vasc. Surg. 2008, 48, 355–361.
40. Trial of carotid stenting vs. carotid endarterectomy. Stroke. 2001, 32, 325 [abstract].
41. Zaidat O., Klucznik R., Alexander M. et al. NIH Multi Center Wingspan Intracranial Stent Registry Study Group. The NIH registry on use of the Wingspan stent for symptomatic 70–99% intracranial arterial stenosis. Neurology. 2008, 70, 1518–1524.