ISSN 1727-818X

International Journal of Interventional Cardioangiology

№33
2013

Read in the Journal:

RUSSIAN SOCIETY OF INTERVENTIONAL CARDIOANGIOLOGY

ISSN 1727-818X

INTERNATIONAL JOURNAL OF INTERVENTIONAL CARDIOANGIOLOGY

№ 33-2013

"International Journal of Interventional Cardioangiology". peer-reviewed scientific and practical journal. Founded in 2002.

Website: www.ijic.ru

Address of the Editions:
101000, Moscow,
Sverchkov per., 5
Phone (+7 495) 624 96 36
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Translation:
Translation bureau
MEDTRAN

Prepared by:
VIDAR Publishing House

Computer makeup:
Yu. Kushel

Corrector:
N. Sheludiakova

Special gratitude to
George Guiguineishvili,
doctor and artist,
for the offered opportunity
to put the photocopy
of his painting
"Interventional
Cardioangiology"
on the cover
of the magazine

ISSN 1727-818X
9 771727 818001

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Structure of the article: (1) Title page; **(2)** Condensed abstract and keywords; **(3)** Structured abstract; **(4)** List of abbreviations; **(5)** Text; **(6)** Acknowledgements (if applicable); **(7)** References; **(8)** Legends for figures; **(9)** Tables. The pagination should start from the title page.

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Contents

Percutaneous Coronary Interventions in Patients with Left Main Coronary Artery Disease: Experience of the Hospital without On-Site Cardiac Surgery

I.S. Bessonov, I.P. Zyryanov, V.A. Kuznetsov, S.S. Sapozhnikov, E.P. Samoylova, E.A. Gorbatenko*

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Feasibility of PCIs in the hospital without on-site cardiac surgery was investigated in 70 patients with LMCA disease. The in-hospital and long-term results were analyzed. The factors affecting the long-term results were determined. The collected data made it possible to conclude that PCIs in this population are effective and relatively safe to be performed in the hospital without on-site cardiac surgery.

Key words: *percutaneous coronary interventions, left main coronary artery, hospital without on-site cardiac surgery.*

Objective. To assess the effectiveness and safety of PCIs in patients with LMCA disease in the hospital without on-site cardiac surgery.

Rationale. The safety of PCIs in facilities without on-site cardiac surgery is currently proven. However, feasibility of PCIs in case of LMCA disease in these facilities is not fully investigated.

Methods. From February 2006 till July 2012, percutaneous coronary interventions were performed in 70 patients with unprotected LMCA disease. The long-tem results from 62 (92.5%) patients were analyzed. Mean follow-up duration was 36.7±2.7 months.

Results. 65 patients had elective interventions and 5 subjects had primary angioplasty. Drug-eluting stents were used in 95% of cases. The major adverse cardiovascular events (MACE) were observed in 15 (23.1%) patients. 10 (15.4%) patients died during follow-up. LMCA in-stent restenosis was observed in 2 (3.1%) cases. Acute myocardial infarction and unstable angina were observed in 6 (9.2%) and 2 (4.6%) patients, respectively. Repeat revascularization was performed in 3 (4.6%) subjects. The major adverse cardiovascular events (MACE) were associated with acute coronary syndrome (RR 5.4; 95% CI 1.3–22.6, p = 0.02) and increased SYNTAX score (RR 1.1; 95% CI 1.01–1.19, p = 0.03).

Conclusions. PCIs in patients with LMCA disease are relatively safe and effective treatment option for CHD and may be performed in the facility without on-site cardiac surgery if patients are carefully selected, intervened by experienced surgeons, and there is the possibility to urgently transfer a patient to the facility with on-site cardiac surgery, if needed. The primary independent predictors of adverse cardiac events are acute coronary syndrome and SYNTAX score.

Abbreviations

CABG – coronary artery bypass grafting
IVUS – intravascular ultrasound
CHD – coronary heart disease
LCA – left coronary artery
ACS – acute coronary syndrome
LAD – left anterior descending artery
PCI – percutaneous coronary intervention

Coronaroangiography reveals the hemodynamically significant disease of the left main coronary artery (LMCA) in 3–7% of cases and this condition is an absolute indication for revascularization (1, 2, 3). Until recently, direct myocardial revascularization was considered to be preferable treatment option for LCMA atherosclerotic disease (4). However, percutaneous coronary interventions (PCIs) demonstrated similar effectiveness in these subjects (5). Elective PCIs performed in the facility without on-site cardiac surgery were proven to be safe and the number of complications does not

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Manuscript received on April 30, 2013
Accepted for publication on May 16, 2013

exceed the rates observed in the facilities with on-site cardiac surgery (6). In real clinical practice, delayed intervention for LMCA disease may be fatal in patients who have no possibility to be operated in timely manner in the facility possessing both cath lab and on-site cardiac surgery. Nevertheless, only some cath labs worldwide have experience in LMCA stenting in the setting without on-site cardiac surgery. Therefore, the objective of this study was to assess the effectiveness and safety of PCIs in patients with LMCA disease in the facility without on-site cardiac surgery.

Material and methods

70 patients with unprotected LMCA disease underwent percutaneous coronary interventions from February 2006 till July 2012.

The analysis included patients with stable and unstable angina, acute myocardial infarction associated with hemodynamically significant stenosis (>50%) of the LMCA. The patients with protected LMCA stenosis, i. e. those with functional grafts to the left coronary artery, were excluded.

The percutaneous coronary interventions were performed using transfemoral and transradial approaches. Aspirin 100 mg/day and clopidogrel 75 mg were proscribed to all patients prior to intervention. In case of primary angioplasty, a loading dose of clopidogrel 600 mg was given. During intervention, unfractionated heparin 70 U/kg was administered as intraarterial bolus; if coronary spasm occurred, nitroglycerin 200 μg was given. In several cases, IIb/IIIa receptor blockers were used during PCI. After completed interventions, all patients received dual desaggregant therapy (aspirin 100 mg/day, clopidogrel 75 mg/day) for at least one year.

The coronarograms were quantitatively analyzed using Phillips Integris Allura equipment (Netherlands). Pre-intervention minimal vessel diameter, post-intervention minimal vessel diameter, stenosis length, percentage of stenosed vessel diameter were determined. 5 patients had intravascular ultrasound (IVUS) using Volcano S5i equipment (USA). Prior to IVUS, all patients received nitroglycerin 200 μg, and the probe was automatically moved at a rate of 0.5 mm/sec.

In case of ostial or middle segment lesions of the LMCA, direct stenting was performed; if the stent could not be passed through the stenosis directly, the stenting was performed after predilatation. In case of LMCA bifurcation lesion, the stent was always implanted covering the left anterior descending artery when the circumflex artery was protected with the wire previously placed in it. If residual stenosis of the circumflex artery exceeded 70%, provisional T-stenting was used passing the wire though the mesh of implanted stent and performing final kissing dilatation. In some cases of extended ostial stenosis of the circumflex artery, modified T-stenting was used. Firstly, stent was placed in the orifice of the circumflex artery, followed by LMCA stenting through the previously implanted stent, and the intervention was finished by kissing dilatation.

According to the European Bifurcation Club guidelines (7), Medina classification was used to classify bifurcation lesions.

The severity of coronary lesions was rated by SYNTAX scale. According to this scale, the predefined number of points were assigned to each affected coronary artery in accordance with its contribution to the blood supply of the left ventricle myocardium. In addition, such factors as occlusion, tri- and bifurcation lesions, arterial tortuosity, stenosis length, calcification, intraluminal thrombus, ostial lesion, and diffuse coronary disease were assessed quantitatively. In case of total occlusion, tri- and bifurcation lesion, some additional characteristics were assessed quantitatively.

The long-tem results from 62 (92.5%) patients were analyzed. Mean follow-up duration was 36.7 ± 2.7 months. 29 (46.8%) patients had control coronarography during follow-up.

Statistical processing was performed using statistical software package (SPSS Inc., version 17.0). The values were presented as M ± m. The distribution of variables was determined using Kolmogorov-Smirnov test. The Cox stepwise proportional hazard regression model was used to assess the relationship between risk factors and adverse cardiocerebral events.

Results

65 patients had elective interventions and 5 subjects had primary angioplasty. LMCA disease was infarct-related in all emergency cases. Following 2011, all interventions (5 PCIs) were performed using transradial approach and intravascular ultrasound.

After LMCA intervention, 9 (12.9%) patients had simultaneous coronary angioplasty for stenoses of other coronary arteries. Thus, 7 (10%) patients had simultaneous stenting for the left anterior descending artery (LAD) steno-

sis and for one case each of the circumflex artery, right coronary artery, and obtuse marginal branch stenoses.

It should be noted, that 10 (14.3%) patients had previous PCIs for coronary atherosclerosis and 13 stents with antiproliferative coating were implanted.

The following stents with antiproliferative coating were mostly used for LMCA angioplasty: Cypher (Cordis), Taxus Liberte monorail (Boston Scientific), Endeavor Sprint (Medtronic), Endeavor Resolut RX (Medtronic), Promus (Boston Scientific), Promus Element (Boston Scientific), Taxus Element (Boston Scientific).

Mean diameter of implanted stents was 3.7 ± 0.04 mm, and mean length was 14.3 ± 0.62 mm. The stents were implanted at high pressure (mean value was 14.6 ± 0.22 atm) in all subjects.

The clinical characteristics of patients are presented in Table 1.

The right-sided coronary blood flow type was detected in the majority of patients (Table 2). Both isolated LMCA disease and LMCA disease combined with one-, two- or multivessel stenoses were observed in investigated arms. The LMCA stenosis varied mostly from 75% to 90% of vessel diameter. In the vast majority of cases LMCA disease was bifurcational.

Table 3 shows characteristics of performed interventions.

Immediate angiographic success was achieved in 95.7% of cases. Three patients with acute coronary syndrome complicated with cardiogenic shock died during endovascular revascularization.

In-hospital period in two patients (2.9%) was complicated with periprocedural myocardial infarction (non-Q-wave myocardial infarction)

Table 1. Clinical characteristics of patients

Parameters	Number of patients	
	Abs.	%
Age (years)	55.5 ± 1.1	
Males	56	80
Smokers	24	36.4
Obesity	47	70.1
Diabetes mellitus	12	17.9
Acute coronary syndrome	12	17.1
Exertional angina		
FC I	4	8.5
FC II	13	27.7
FC III	29	61.7
FC IV	1	2.1
History of arterial hypertension	57	85.1
Previous myocardial infarction	25	37.3
Circulatory failure		
FC I	14	21.2
FC II	41	62.1
FC III	11	16.7
Total cholesterol (mmol/L)	5.1 ± 0.2	

Table 2. Angiographic characteristics of patients

Parameters		Number of patients	
		Abs.	%
Type of coronary blood flow			
	Right-sided	58	82.9
	Left-sided	12	17.1
Number of affected coronary arteries			
	LMCA only	26	38.8
	LMCA + 1 CA*	28	41.8
	LMCA + ⩾2 CA	13	19.4
Stenosis diameter, %			
	50–75%	8	11.4
	75–90%	41	58.6
	>90 %	2	2.9
	Subtotal stenosis	16	22.9
	Occlusion	3	4.3
Stenosis length, mm		11.4 ± 0.5	
Localization of LMCA disease			
	Ostial	5	7.1
	Middle segment	14	20
	Distal parts	51	72.9
Type of bifurcational lesion			
	1,1,1	38	74.5
	1,1,0	6	11.8
	1,0,1	5	9.8
	1,0,0	1	2
	0,1,0	1	2
Mean SYNTAX score		18.9 ± 0.8	

*CA – coronary artery.

Table 3. Characteristics of performed interventions

Parameters	Number of patients	
	Abs.	%
Isolated LMCA stenting	60	85.7
LMCA stenting + left anterior descendent artery stenting	7	10
LMCA stenting + circumflex artery stenting	1	1.4
LMCA stenting + right coronary artery stenting	1	1.4
LMCA stenting + obtuse marginal branch stenting	1	1.4
Transradial approach	5	7.1
Primary PCI in ACS	5	7.1
Application of IIbIIIa receptor blockers	4	5.7
Intravascular ultrasound	5	7.1
Technique of LMCA stenting in case of bifurcation lesion		
One stent	32	64
provisional T-stenting	11	22
modified T-stenting	7	14
Number of implanted stents without antiproliferative coating		
Multilink Zeta (Guidant)	1	1.3
Multilink Vision (Guidant)	2	2.6
Liberty (Boston Scientific)	1	1.3
Number of implanted stents with antiproliferative coating		
Cypher (Cordis)	28	36.8
Taxus Liberte monorail (Boston Scientific)	15	19.7
Endeavor Sprint (Medtronic)	6	7.9
Promus (Boston Scientific)	5	6.6
XinceV (Abbott Vascular)	6	7.9
Endeavor Resolut RX (Medtronic)	1	1.3
Promus Element (Boston Scientific)	9	11.8
Taxus Element (Boston Scientific)	2	2.6
LMCA diameter, mm		
Pre-interventional	0.7 ± 0.06	
Post-interventional	3.7 ± 0.06	
Mean stent diameter, mm	3.7 ± 0.04	
Mean stent length, mm	14.2 ± 0.5	
Mean pressure of stent implantation, atm	14.6 ± 0.22	

Table 4. Long-term results

Parameters	Number of patients	
	Abs.	%
Follow-up (months)	36.7 ± 2.7	
Major adverse cardiovascular events (MACE)	15	23.1
Death	10	15.4
Myocardial infarction	6	9.2
Repeat revascularization	3	4.6
Unstable angina	3	4.6
LMCA in-stent restenosis	2	3.1

associated with 3-fold increase in markers of myocardial necrosis (troponin T and CPK-MB) without clinical symptoms and specific electrocardiographic changes. Control coronarography performed in these patients revealed no evidence of in-stent thrombosis or coronary occlusion.

The major adverse cardiovascular events (MACE) were observed in 15 (23.1%) patients when the long-term results were analyzed (Table 4). 10 (15.4%) patients died during follow-up. One fatal outcome observed in elective patient was due to voluntary premature discontinuation of dual desaggregant therapy by this patient. LMCA in-stent restenosis was observed in two (3.1%) cases. In these patients, stents with another antiproliferative coating were implanted to suppress intimal proliferation. 2 months after LMCA stenting one patient had elective LAD angioplasty. Anterior-lateral Q-wave myocardial infarction associated with specific electrocardiographic pattern developed 2 hours after the procedure. Control coronarography revealed acute LAD in-stent thrombosis and balloon angioplasty of the infarct-related artery was performed. One

patient had acute gastrointestinal bleeding. Thus, endoscopic hemostasis was performed, and short-term interruption of clopidogrel intake was recommended.

Percentage of patients with no clinical evidence of angina pectoris during follow-up was 32.7%.

After multivariate analysis, the major adverse cardiovascular events (MACE) were associated with acute coronary syndrome (RR 5.4; 95% CI 1.3-22.6, p = 0.02) and increased SYNTAX score (RR 1.1; 95% CI 1.01–1.19, p = 0.03).

Discussion

The safety issues of percutaneous coronary interventions performed at the facility without on-site cardiac surgery have been discussed for a long time. Modern guidelines classify these interventions as Class IIb (available data mainly show usefulness/effectiveness of the treatment). However, National Cardiovascular Data Registry (6) (USA) covering more than 300,000 PCIs demonstrated no differences in rates of mortality, non-fatal myocardial infarction, and necessity of emergency coronary artery bypass grafting between patients intervened in facilities without on-site cardiac surgery and facilities with on-site cardiac surgery. This information was confirmed by recently published data from the randomized study including 3691 patients (8). Over the last decades, the trend to reduced necessity of emergency coronary artery bypass grafting in case of elective PCIs was observed (9). This is explained by improvement of medical technologies and pharmacological support. It should be noted that there were no patients requiring emergency transportation for direct myocardial revascularization in our study.

The collected data demonstrated that acute coronary syndrome in LMCA patients is characterized with unfavorable prognosis. Totally, 7 deaths out of 10 fatal outcomes observed during follow-up (36.7 ± 2.7 months) occurred in ACS patients. LMCA disease was infarct-related in all cases. J.Hurtado et al. (10) have also demonstrated high procedural (16%) and in-hospital (47%) mortality in patients with ACS and infarct-related LMCA disease. Moreover, large ACS registry, AMIS Plus (11) covering more than 6500 patients determined that LMCA disease in ACS is an independent predictor for in-hospital mortality (OR = 2.36; 95% CI:1.34–4.17; p = 0.003). It should be noted that modern guidelines allow percutaneous coronary interventions including LMCA interventions to be performed in ACS patients in facilities without cardiac surgery on site (Class IIA) (12).

PCIs in elective patients with LMCA disease are performed only after careful patient selection. Weighted decision making on preferable revascularization option plays an important role. In our study, the decision on revascularization method in elective patients was made by council of physicians including cardiologist, endovascular surgeon, and cardiovascular surgeon. In our facility, the protocol was approved for emergency transportation of patients to the facility with on-site cardiac surgery (distance of 10 kilometers), if needed.

Lesion localization has significant influence on PCI results when LMCA disease is intervened. From the technical point of view, ostial stenting or stenting of middle part of the LMCA is simpler than intervention in distal part of the LMCA (13). Moreover, PCI for bifurcation LMCA disease is associated with increased rate of restenoses (14) confirming the data from our study. It is possibly related to more complicated stenting methods requiring two stents to be implanted. Thus, after 2-year follow-up patients who were implanted with one stent for LMCA disease had reduced rate of major adverse cardiovascular events (24.7% versus 32.4%, p = 0.02) including repeat myocardial revascularization rate (13.0% versus 26.9%, p = 0.00001) compared with patients who had two implanted stents (15). Moreover, the severity of coronary lesion has an important role when patients are selected for PCI. Based on 5-year follow-up data, SYNTAX trial (5) demonstrated that PCI in patients with LMCA disease is reasonable provided that SYNTAX score is <32. If SYNTAX score was high (>32), CABG was associated with lower rate of major adverse cardio-cerebral events (MACCE) compared to PCI (42.6% versus 26.3%, p < 0.003). These data confirmed our results that SYNTAX score was an independent predictor for adverse cardiovascular events in the long-term period.

Conclusions

1. Percutaneous coronary interventions in patients with LMCA lesions are relatively safe and effective for CHD.

2. The main independent predictors for adverse cardiac events are acute coronary syndrome and SYNTAX score.

3. Percutaneous coronary interventions performed in the facility without on-site cardiac

surgery are allowed if patients are carefully selected and intervened by experienced surgeon and there is the possibility to urgently transfer a patient to the facility with on-site cardiac surgery, if needed.

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Advisability of Incomplete Multivessel Revascularization in Patients with *ST*-Elevation Myocardial Infarction and Multivessel Coronary Artery Disease

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There are some strategic issues regarding the treatment of patients with ST-segment elevation myocardial infarction at multivessel coronary artery disease which are not completely solved. In particular, evidential base for multivessel stenting within the scope of primary percutaneous coronary intervention is controversial. This may be related to the absence of guidelines regulating advisability of complete and incomplete revascularization in this group of patients. Strategies of reasonable complete and incomplete revascularization in patients with ST-segment elevation myocardial infarction undergoing multivessel stenting have been comparatively analyzed in this study.

Key words: *myocardial infarction, incomplete myocardial revascularization, multivessel lesion, multivessel stenting.*

Objective. To assess criteria of reasonable incomplete multivessel revascularization in the population of patients with *ST*-segment elevation myocardial infarction (STEMI) and multivessel coronary artery disease (MVCAD).

Materials and methods. Thirty-day and long-term outcomes of multivessel revascularization with percutaneous coronary interventions (PCI) were analyzed in 159 patients with STEMI and MVCAD. The first group comprised patients who underwent complete reasonable revascularization (CR) within the scope of multivessel stenting at primary PCI or staged approach (n = 114); the second group consisted of patients with so called reasonable incomplete revascularization (IR) after multivessel stenting or staged PCI (n = 45). In all cases IR was acknowledged reasonable due to the presence of corresponding anatomic and/or functional criteria used in the literature: small arterial diameter (<2.5 mm), maximum one non-revascularized epicardial vessel, stenoses in the secondary branches in case of oligosymptomatic course of the disease, unviable myocardium or a small volume of viable myocardium in the blood supply area of an artery [1, 5, 6, 9].

Results. Patients from the studied groups were comparable in the main clinico-demographic and angiographic parameters, revascularization strategies and PCI peculiarities. Both during 30-day follow-up and in the remote period (12 months), no differences were observed between CR and IR groups in the incidence of adverse cardiovascular events (death, repeated myocardial infarction, repeated target vessel revascularization (TVR), composite endpoint).

Conclusion. In the cohort of STEMI patients with multiple coronary artery disease who underwent multivessel stenting within the scope of primary PCI or staged PCI, reasonable incomplete myocardial revascularization is a justified approach which does not increase the incidence of adverse cardiovascular events during 12-month follow-up as compared to the patients who underwent reasonable complete revascularization.

Abbreviations

STEMI – *ST*-segment elevation myocardial infarction
MI – myocardial infarction
ST – stent thrombosis
ML – multivessel lesion
PCI – percutaneous coronary intervention
MS – multivessel stenting
CR – complete revascularization
IR – incomplete revascularization
SR – staged revascularization
LVEF – left ventricular ejection fraction
PICS – postinfarction cardiosclerosis

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Manuscript received on April 17, 2013
Accepted for publication on May 27, 2013

IRA – infarct-related artery
Non-IRA – non-infarct-related artery
TVR – target vessel revascularization
Non-TVR – non target vessel revascularization

Introduction

According to the literature data, incomplete coronary revascularization may result in the increased risk of death, myocardial infarction, repeated revascularization and angina worsening the quality of life (1). However, a certain part of evidential base for this postulate was obtained from the studies conducted in the 80s of the XXth century. Thus, 15% reduction of 5-year mortality in cardiac surgery was demonstrated in patients with complete revascularization (CR) versus incomplete revascularization (2, 3). This hypothesis was also acknowledged when using percutaneous coronary interventions (PCI). Increase of IR-associated mortality during PCI was registered in the New York Register, and IR resulted in increased necessity to perform coronary artery bypass grafting in the Arterial Revascularization Therapies Study (ARTS) (4–6). In one more study, IR resulted in increased left ventricular contractility which was considered to be one of the prognosis-improving mechanisms (7).

Despite the above data on the negative role of IR, results of several modern studies doubt their legitimacy. In the Asan Medical Center Multivessel Registry, no differences in the incidence of adverse cardiovascular events depending on revascularization degree were demonstrated during 5 years in 1914 patients with multivessel lesions who underwent coronary artery bypass grafting or PCI with drug-eluting stents (8). Nevertheless, a significant increase in the incidence of adverse events during the remote follow-up period was observed in about 20% of patients from IR group which indicates the necessity to develop precise criteria of reasonable IR and rational CR.

It should be noted that up to date there is no generally accepted definition and final criteria of IR. Nevertheless, the following definitions are most commonly used: IR is defined as any non-revascularized vessel with >1.5 mm diameter and 50% to 100% stenosis (6, 9), or any artery with >70% stenosis (5), or any artery with 1.5–2 mm diameter and 50% to 100% stenosis (1).

IR is most commonly observed in patients after PCI as compared to patients who underwent coronary artery bypass grafting (59% and 33%, respectively) (1). According to other authors, IR takes place in 45–89% of cases during stenting of multivessel arterial lesions (5).

The term “reasonable incomplete revascularization” appeared over the last years (1, 10). Legitimacy of such definition was confirmed in a number of modern studies. Thus, no differences in functional status, death rate and myocardial infarction rate were obtained within 1 year after PCI and coronary artery bypass grafting in SYNTAX study (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) despite the lower incidence of CR in PCI group (56.7% versus 63.2%, p = 0.005) (9, 11). Outcomes of CR and IR with PCI conducted due to bifurcation stenoses were compared in another study. Stenting of both main and side branches with >2 mm diameter was conducted in a group of patients with CR, while patients from IR cohort underwent only stenting of the main vessel. As a result, no advantages of CR over IR were registered; moreover, a potential harm of total blood flow restoration was demonstrated (12).

The term “reasonable incomplete revascularization" in the literature means situations in which IR is not associated with increased risk of adverse cardiovascular events. Moreover, there are corresponding anatomic, functional and physiological criteria. For example, anatomic criteria of reasonable IR include small diameter of an artery (<2.5 mm), maximum one non-revascularized epicardial vessel and stenoses in the secondary branches in case of oligosymptomatic course of the disease. Functional criteria include unviable myocardium or a small volume of viable myocardium in the blood supply area of an artery; meanwhile, fractional flow reserve >0.80 is referred to physiologic ones (1).

Thus, there is no final solution to a problem of determining CR advisability in various clinical and anatomic situations. Main literature data and studies on this topic concern the patients with stable CHD and multivessel lesions, while revascularization approaches in myocardial infarction patients with multiple stenoses of the coronary vessels are not covered enough. Hence, objective of this study was to assess criteria of reasonable incomplete multivessel revascularization in STEMI patients with multiple coronary artery disease.

Materials and methods

Data from a registrational study conducted in accordance with Good Clinical Practice guidelines and Declaration of Helsinki principles served as material for this analysis. Study pro-

Table1. Clinical and demographic characteristics

Parameter	Complete revascularization (n = 114)	Incomplete revascularization (n = 45)
Age	57.6 ± 9.5	62.6 ± 10.0
Male gender	66.6% (76/114)	64.4% (29/45)
LVEF	51.9 ± 7.8%	49.4 ± 7.8%
Arterial hypertension	88.6% (111/114)	91.1% (41/45)
Diabetes mellitus	22.8% (26/114)	22.2% (10/45)
Multifocal atherosclerosis	21% (24/114)	26.6% (12/45)
Postinfarction cardiosclerosis	11.4% (13/114)	11.1% (5/45)
Residual manifestations of cerebrovascular accident	3.5% (4/114)	2.2% (1/45)
Killip II acute heart failure	9.6% (11/114)	11.1% (5/45)

No statistically significant differences were observed between parameters.

tocol has been approved by the Ethics Committee of Scientific Research Institute. Inclusion criteria were as follows: 1. STEMI with duration <12 hours and primary PCI. 2. Hemodynamically significant lesions (⩾70%) of two and more coronary arteries. 3. Multivessel stenting within the scope of primary PCI or staged approach. Exclusion criteria: 1. Killip III–IV acute heart failure. 2. Left main coronary artery disease with ⩾50% stenosis. Standard double antiplatelet therapy was prescribed to all patients for at least 12 months.

The patients were assigned into two groups. The first group comprised patients who underwent reasonable CR within the scope of multivessel stenting at primary PCI or staged approach (n = 114); the second group consisted of patients with IR after multivessel stenting or staged PCI (n = 45). In all cases, IR was acknowledged reasonable due to the presence of corresponding anatomic and/or functional criteria used in the literature: small arterial diameter (<2.5 mm), maximum one non-revascularized epicardial vessel, stenoses in the secondary branches in case of oligosymptomatic course of the disease, unviable myocardium or a small volume of viable myocardium in the blood supply area of an artery (1).

Study endpoints within 30 days after myocardial infarction and in the remote period (12 months) included death, repeated myocardial infarction (MI) and repeated target vessel revascularization (TVR); composite endpoint event rate including death, MI and TVR was also assessed. Certain stent thrombosis (ST) was studied throughout the whole observation according to generally accepted Academic Research Consortium (ARC) classification. Evaluation of 30-day and long-term results was conducted using clinical data collected at the patient's visit to the clinic or during the telephone interview. Descriptive part of results was presented by mean ± standard deviation. Qualitative parameters were compared with the use of χ^2 test. In case of normal distribution, univariate analysis of variance (ANOVA) was used for quantitative data comparison between groups. The differences were considered statistically significant at $p < 0.05$. Study results were processed with the use of the software package Statistica for Windows 6.0 (StatSoft Inc., USA).

Groups of CR and IR patients were also comparable in the main clinico-demographic parameters (Table 1).

CR and IR groups were comparable in the main angiographic parameters, including severity of coronary lesions according to SYNTAX scale, description, quantity and basic characteristics of implanted stents, the volume of used radiopaque contrast agent and radiation dose. Drug-eluting stents were used in more the half of cases both during intervention on the IRA and during stenting of the non-IRA.

Multivessel stenting within the scope of primary PCI or staged approach were used as revascularization strategies in both groups. Groups did not differ in success rate of intervention on the IRA which was defined as at least TIMI 3 final blood flow with no significant complications (Table 3).

Thus, the patients from the studied groups were similar in demographic parameters, clinical status and concomitant pathology. Mean parameter of coronary lesion severity in both groups was low (SYNTAX score ⩽22). In all cases, complete revascularization in IR group was considered unreasonable in accordance with anatomic and/or functional criteria. In 12 patients (26.6%), advisability of IR was dictated

Table 2. Angiographic characteristics of patients and implanted stents in the groups of patients

Parameter	Complete revascularization (n = 114)	Incomplete revascularization (n = 45)
Syntax score	17.8 ± 7.2	22.2±8.2
The volume of radiopaque agent, mL	307.7 ± 120.5	324.4 ± 155.1
Radiation dose, mGy	3336.6 ± 1704.9	3019.5 ± 1378
Drug-eluting stents in the IRA	51.7% (59/114)	53.3% (24/45)
Mean number of stents in the IRA	1.3 ± 0.5	1.4 ± 0.6
Drug-eluting stents in the non-IRA	71% (81/114)	82.2% (37/45)
Mean number of stents in the non-IRA	1.3 ± 0.5	1.1 ± 0.4
Mean stent length in the IRA, mm	28.9 ± 11	28.3 ± 12.6
Mean stent diameter in the IRA, mm	3.3 ± 0.6	3.3 ± 0.6
Mean stent length in the non-IRA, mm	25.1 ± 12.3	19.9 ± 7.8
Mean stent diameter in the non-IRA, mm	3.2 ± 0.5	3.1 ± 0.7

No statistically significant differences were observed between parameters.

Table 3. Success rate and peculiarities of revascularization in the groups of patients

Parameter	Complete revascularization (n = 114)	Incomplete revascularization (n = 45)
Multivessel stenting	47.4% (54/114)	35.5% (16/45)
Staged revascularization	52.6% (60/114)	64.5% (29/45)
Successful PCI of the IRA	97.4% (111/114)	97.7% (44/45)
Successful PCI of the non-IRA	99.1% (113/114)	97.7% (44/45)
Mean time period between revascularization stages, days	79.6 ± 99.3	95.8 ± 124.1

No statistically significant differences were observed between parameters.

Table 4. Thirty-day outcomes in the groups of patients

Parameter	Complete revascularization (n = 114)	Incomplete revascularization (n = 45)
Death	1.75% (2)	0% (0)
Myocardial infarction	0.9% (1)	0% (0)
TVR (urgent)	0.9% (1)	0% (0)
Stent thrombosis	0.9% (1)	0% (0)
Composite endpoint (death + myocardial infarction + TVR (urgent))	3.5% (4)	0% (0)

No statistically significant differences were observed between parameters.

by the presence of chronic occlusion in one coronary artery with intra- and/or intersystemic collaterals and asymptomatic course of CHD after multivessel stenting or maximum first functional class of exertional angina. In 33 cases (73.4%), IR was reasonable due to >70% stenosis of the coronary artery 2–2.5 mm in diameter with asymptomatic course of CHD after multivessel stenting or maximum first functional class of exertional angina. In the majority of cases, drug-eluting stents and two-stage approach were used with high success rate of the intervention both on the IRA and non-IRA.

Results

Results of 30-day follow-up are rather topical: firstly, due to the fact that STEMI patients who underwent revascularizaiton with primary PCI served as study subjects, and secondly, due to significant number of patients with multivessel stenting within the scope of primary procedure (35.5–47.4%). No statistically significant differences were observed between groups in the event rate of such endpoints as death, repeated MI, TVR, or composite endpoint including death, MI and TVR. No adverse cardiovascular events were registered in IR

Table 5. One-year outcomes in the groups of patients

Parameter	Complete revascularization (n = 114)	Incomplete revascularization (n = 45)
Death	2.6% (3)	0% (0)
Myocardial infarction	0.9% (1)	2.2% (1)
TVR (urgent)	1.75% (2)	0% (0)
Stent thrombosis	1.75% (2)	0% (0)
Composite endpoint (death + myocardial infarction + TVR (urgent))	5.3% (6)	2.2% (1)

No statistically significant differences were observed between parameters.

group, while a case of ST which required urgent intervention on the target vessel leading to recurrence of MI and death was observed in CR group. The second case of patient's death in this group was caused by unsuccessful intervention on the IRA and stenting of only non-IRA which resulted in lethal outcome due to hemotamponade on Day 2 from the disease onset. (Table 4).

Long-term outcomes were assessed 12 months after the index event. There were no statistically significant differences between groups of patients. It should be noted that the number of death cases in CR group increased due to one more case of lethal outcome caused by oncologic disease 9 months after revascularization which was diagnosed after the patient's discharge from the clinic. In the remote follow-up period, one more ST episode occurred in CR group which did not result in repeated MI but required TVR. The structure of composite endpoint by Month 12 of the follow-up with 5.3% event rate consisted of 3 death cases (2 cardiac and 1 non-cardiac), one repeated MI and two cases of urgent repeated intervention on the target arteries. No lethal outcomes and TVR were observed in IR group for 12 months. One non-fatal intraoperative MI caused by unsuccessful PCI on the non-IRA (second stage of revascularization) took place. Composite endpoint event rate in this group was 2.2% (Table 5).

Discussion

In conducted study of 159 STEMI patients with multiple coronary artery disease, the rate of reasonable IR was 28.3% which is somewhat lower as compared to published data (45–89% (5)) and may be related on one hand to the fact that 100% of patients both from CR and IR groups underwent multivessel stenting either within the scope of primary PCI or during the staged approach. On the other hand, we used a coronary artery diameter of 2–2.5 mm as one of reasonable IR criteria since it potentially makes possible a stent implantation, while some investigators use vessel diameter of >1.5 mm or 1.5–2 mm as such criterion (1, 6, 9). In our opinion, the use of such anatomic criterion as 2–2.5 mm arterial diameter in this study was reasonable because exactly such vessel caliber often creates a dilemma for interventional cardiologist during multivessel stenting within the scope of primary PCI or staged approach. Besides, such parameter does not contradict published data (5, 6, 9).

Multivessel stenting strategy within the scope of primary PCI has contradictory evidential base (13); nevertheless, we successfully implemented it in 70 patients which constituted 44% out of total number of patients. This approach to myocardial revascularization in STEMI patients seems rather promising which is related to the absence of increased risk of adverse events during PCI conducted not only on the IRA but on the non-IRA as well within the scope of primary PCI. On the other hand, uncertainty regarding the type, the scope and the time of revascularization of vessels not directly related to the infarction area, as well as low availability of the second stage of revascularization in real clinical practice makes MS strategy one of the options in solving this problem (13).

If, besides the lesion of the IRA and at least of one more significant vessel, STEMI patients considered as candidates for multivessel stenting within the scope of primary PCI or staged approach have ⩾70% stenoses in the coronary arteries with 2–2.5 mm diameter or chronic occlusion with formed collaterals, this often complicates decision-making on the scope of revascularization. In relation to this, development of revascularization advisability criteria in this cohort of patients seems to be a rather topical issue.

Overwhelming majority of studies investigating this problem are orientated towards the

patients with stable CHD, while there is not enough works aimed at solving the tasks related to the choice of revascularization strategy in MI with multiple coronary artery disease despite the fact that this is the case in more than a half of STEMI patients (14).

Objective of this study was to investigate the possibility of using reasonable IR criteria for the cohort of STEMI patients. Standards which proved their efficacy in a group of stable patients were used as a guide (1, 5, 6, 9).

Obtained results demonstrated prospects of using IR advisability criteria in the group of MI patients as well. 30-day and long-term results demonstrated that IR may become an option for patients who have, besides the lesion of IRA and at least of one more significant vessel, ⩾70% stenoses of small coronary arteries (2–2.5 mm in diameter) or chronic occlusion and formed collaterals and who undergo revascularization within the scope of multivessel stenting at primary PCI or staged approach. Non-performance of intervention on small caliber arteries or chronic occlusions after implementing multivessel strategy in case of asymptomatic or oligosymptomatic CHD was not accompanied by increased incidence of adverse cardiovascular events as compared to the group of reasonable CR. Event rate of composite endpoint including death, repeated MI and TVR during 12 months was 2.2% versus 5.3% in IR and CR groups, respectively ($p > 0.05$).

Low incidence of adverse cardiovascular events in the studied cohort of STEMI patient as compared to published data (15) may be explained by a number of factors: firstly, the study design implied exclusion of patients with severe acute heart failure and left main coronary artery disease; secondly, all patients underwent multivessel stenting within the scope of one of revascularization strategies with the use of drug-eluting stents in more than a half of cases.

Thus, the main result of conducted study consisted in obtaining data confirming possibility of effective use of reasonable IR criteria in the cohort of STEMI patients without pronounced acute heart failure. This scenario will help to achieve satisfactory results in treating patients without unreasonable risk related to additional invasive intervention.

Conclusion

Problems regarding the choice of PCI strategy, time and degree of myocardial revascularization in STEMI with multivessel coronary artery disease are currently not solved and are considered topical both for practicing cardiologists and during scientific search for new knowledge. Uncertainty regarding differentiated approach to myocardial revascularization in STEMI patients pushes us towards the search of objective criteria capable of determining optimal treatment for each specific patient. Multivessel stenting strategy in STEMI patients may be used both within the scope of primary PCI and during the staged approach and seems to be rather promising. Criteria of IR advisability may be effectively implemented also in the group of MI patients to optimize patients' treatment results without unjustified risk related to additional invasive intervention.

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Impact of Myocardial Reperfusion Timing on Immediate and Long-Term Disease Prognosis in Patients with Acute *ST*-Elevation Myocardial Infarction (STEMI)

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From 2001 through 2011, endovascular interventions have been performed in Moscow City Center of Interventional Cardioangiology in 3770 patients with STEMI. Combined thrombolytic and endovascular treatment of the infarct-related artery (IRA) was performed in 1091 cases. We have elaborated and inculcated into the clinical practice the algorithms of diagnostic and therapeutic interventions for STEMI patients allowing the reduction of time for emergency care of such patients. During the described period, the decreased time of myocardial reperfusion in STEMI patients due to broader use of thrombolytics, optimization of organizational measures, including the interaction with emergency care services, allowed to decrease in-hospital mortality from 4,6% to 1,2%, to significantly reduce the rate of MACE. The combination of pre-hospital thrombolytic therapy and endovascular angioplasty provides earlier and fuller correction of the blood flow in the IRA, significantly improvement of in-hospital and long-term prognosis in STEMI patients.

Key words: *acute myocardial infarction, thrombolytic therapy, endovascular procedures.*

Nowadays it is proved that early myocardial reperfusion (within the first 6 hours from the disease onset) is an effective method limiting the damage of cardiac muscle in *ST*-segment elevation acute myocardial infarction (STEMI) (2, 4, 5, 7, 14). It is also known that the earlier blood flow in the infarct-related artery (IRA) is restored, the smaller is necrotic focus in myocardium and apoptosis of cardiomyocytes in the infarct and peri-infarct zones (10, 11). This, in turn, preserves myocardial contractility and prevents left ventricular remodeling processes, thus decreasing mortality rate and the rate of serious cardiac events at the in-hospital stage. According to some authors, early blood flow restoration in the IRA also favorably affects the long-term prognosis in these patients. (1, 2, 5–9, 21).

The earliest myocardial reperfusion may be achieved by prehospital systemic thrombolytic therapy. However, in such situation blood flow in the IRA can be restored only partially, as after thrombus destruction a morphological substrate preventing the flow remains in the IRA (stenotic atherosclerotic plaque), which increases the possibility or rethrombosis, the rate of recurring ischemia and other adverse events.

More adequate blood flow restoration in the IRA may be achieved by endovascular myocardial reperfusion in the in-patient settings; however, it wastes the precious time required for patient's delivery to the in-patient department (10, 11, 26, 27). Meanwhile, randomized studies demonstrated that the longer is the period of patient's delivery and preparation to the endovascular procedure, the less pronounced is clinical effect of myocardial reperfusion and the worse is disease prognosis especially in high-risk patients (12, 15, 36).

Taking into consideration the above-mentioned, it can be assumed that prehospital systemic thrombolysis is the first to restore the blood flow in the IRA; however, blood flow restoration is incomplete due to stenotic atherosclerotic plaque. On the other hand, endovascular myocardial reperfusion provides more complete blood flow restoration in the IRA; however, due to the loss of time required for patient's transportation to the in-patient department and his/her preparation for the procedure, blood flow restoration is conducted significantly later. This served as basis for some investigators,

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Manuscript received on April 25, 2013
Accepted for publication on May 13, 2013

including us, for using combination of two methods mentioned above in the treatment of acute myocardial infarction, i.e. combination of prehospital thrombolytic therapy with subsequent coronary angiography and possible (as indicated) endovascular angioplasty of the IRA (1, 3, 13, 18–20). Such combined reperfusion treatment of AMI makes it possible to achieve the earliest and the most complete correction of the blood flow in the IRA.

Moscow City Center of Interventional Cardioangiology together with Moscow Emergency Care executives pioneered in implementing the above-mentioned complex treatment of patients with acute myocardial infarction (STEMI) into the clinical practice since 2001. For this purpose, large organizational work was conducted on establishing accurate cooperation between different branches of Moscow Emergency Care services and municipal medical preventive facilities. First of all, such interaction is necessary to maximally reduce the time required for patient's delivery to the in-patient department (X-ray operating room). It should be noted that currently there is a complete mutual understanding and coordinated actions between the above-mentioned structures which makes it possible to maximally reduce the time required for patient's delivery and preparation, and to deliver the patient in the operating room already in 20–30 minutes after his/her admission to the in-patient department.

Moscow City Center of Interventional Cardioangiology has experience of using combined thrombolytic and endovascular treatment in a few thousands of STEMI patients. This allowed us to optimize algorithm and work out some methodical recommendations on treatment of STEMI patients.

Objective of this study was to investigate relationship between immediate and long-term prognosis and the timing of reperfusion therapy in STEMI patients.

Clinical characteristics of the patients, methods and study results

For the period from 2001 through 2011 inclusive, endovascular myocardial reperfusion was performed to 3770 STEMI patients in the Moscow City Center of Interventional Cardioangiology. The results of diagnostics and treatment of specified patients in the immediate and mid-term period were retrospectively analyzed with the help of automated system for record-keeping and archiving case history data (DIMOL-IK). Significance of differences in various parameters between the study groups of patients was assessed using non-parametric Mann–Whitney U-test. Changing of parameters over the follow-up period was assessed by Wilcoxon criterion. Correlation analysis was performed using Pearson correlation coefficient. Quantitative variables are presented as M ± m (M – mean statistic value, m – standard error of the mean). Statistical processing of obtained data was performed using Statistica 6.1 software. Differences were considered as significant at $p < 0.05$.

Out of 3770 patients with acute myocardial infarction (AMI) who underwent endovascular myocardial reperfusion, prehospital thrombolysis was performed in 1091 (28.9%) patients. These patients were considered as those who received the earliest myocardial reperfusion. The date and time of angina attack, the time of admission to the in-patient department, the time of endovascular intervention were accurately registered for each patient treated in the Moscow City Center of Interventional Cardioangiology.

Over 80% of patients were younger than 70 years old, most of them were males (79.8%). 16.4% had previous myocardial infarction. Acute left ventricular failure (Killip II–IV), II–III degree AV-block, ventricular fibrillation (VF), paroxysmal atrial fibrillation (Table 1) were observed in 19.7% of patients.

As is evident from Table 1 and Figure 1, hospital mortality rate decreased from 4.6% to 1.2% during the follow-up. Mortality rate was on average 2.3%.

The time between the onset of angina attack and endovascular intervention (pain-to-balloon time) was on average 229.4 ± 48.1 minutes. This parameter included prehospital stage (pain-to-door time – 190.1 ± 31.4 minutes) and time required for preparation and examination of the patient prior to endovascular procedure (door-to-balloon time – 39.3 ± 13.4 minutes). It should be especially noted that throughout the follow-up period these two values decreased: pain-to-door time became 30 minutes shorter, and door-to-balloon time – 17 minutes shorter. Thus, total decrease of time from the disease onset till EVP was 47 minutes (Figure 2).

Endovascular coronary blood flow restoration in a majority of patients (88%) was conducted within 19 to 360 minutes from the disease onset. In the remaining 12% of cases, urgent intervention was conducted later. It should be particularly noted that according to the protocol

Table 1. Main clinical and anamnestic parameters of studied patients with AMI (2001–2011)

Показатель	Year											Mean value
	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	
Number of AMI patients with conducted endovascular procedure (EVP)	151	170	267	302	318	336	403	433	417	392	581	n = 3770
Number of AMI patients with thrombolytic therapy (TLT) + EVP	14 (9.3%)	25 (14.7%)	37 (13.8%)	44 (14.5%)	56 (17.6%)	51 (15.2%)	136 (33.7%)	124 (28.6%)	152 (36.4%)	209 (53.3%)	243 (41.8%)	n = 1091 (28.9%)
Age < 70 years old (%)	79.3	78.0	76.7	81.2	82.2	80.4	79.8	78.4	81.7	82.1	80.4	81.1
Male gender (%)	79.4	77.1	83.8	75.2	78.9	74.4	79.4	76.1	83.3	79.1	81.4	79.8
Myocardial infarction (MI) (in anamnesis) (%)	14.5	15.2	13.8	16.4	17.0	14.7	16.7	16.2	17.2	17.5	15.9	16.4
Complaint-to-door time (minutes)	216 ± 2.4	210 ± 9.7	199 ± 7.4	201 ± 9.2	197 ± 5.2	192 ± 4.7	193 ± 2.1	190 ±29.4	188 ±30.4	187 ± 28.0	186 ± 28.3	190.1 ± 1.4
Door-to-balloon time (minutes)	52 ± 9.4	50 ± 9.1	47 ± 7.3	45 ± 5.4	47 ± 5.7	42 ± 4.6	41 ± 2.4	38 ± 1.3	37 ± 2.9	37 ± 12.2	35 ± 11.5	39.3 ± 13.4
Complaint-to-balloon time (minutes)	268 ± 2.9	260 ± 8.1	246 ± 6.4	246 ± 7.7	244 ± 5.1	234 ± 4.1	234 ± 8.2	228 ± 7.4	225 ± 6.5	224 ± 44.9	221 ± 45.1	229.4 ± 48.1
Complications of AMI (%)	23.5	21.9	21.0	21.1	20.9	20,2	19,8	19,5	18,6	18,4	18,7	19,7
Mortality (%)	4.6	3.5	3.4	3.3	3.4	3,0	2,2	1,9	1,5	1,3	1,2	2,3

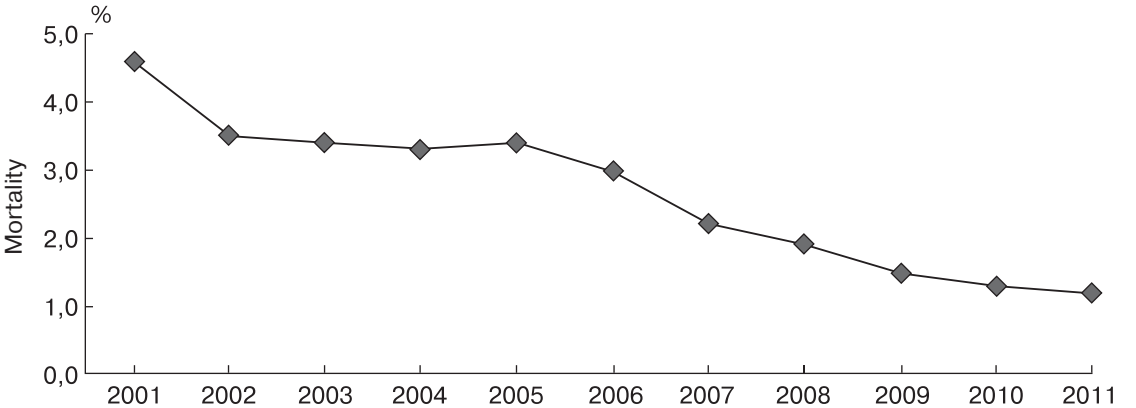

Figure 1. Mortality rate in STEMI patients during the follow-up over time.

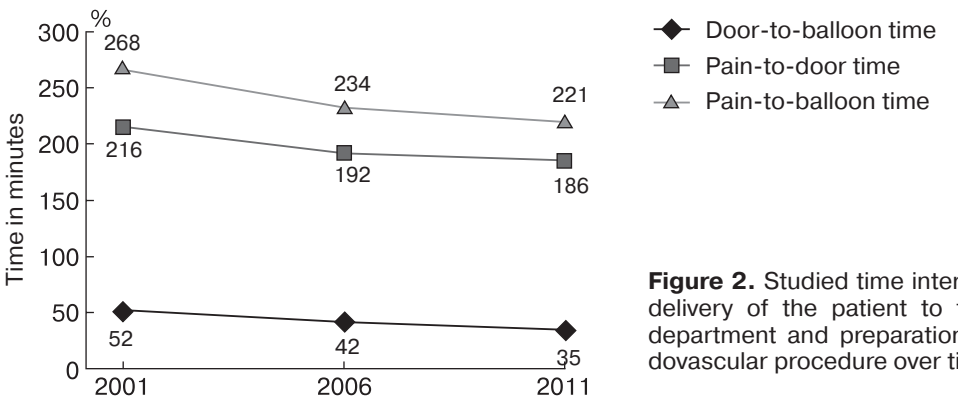

Figure 2. Studied time intervals spent for delivery of the patient to the in-patient department and preparation for radioendovascular procedure over time

adopted in the Moscow City Center of Interventional Cardioangiology, urgent endovascular procedure later than six hours from the angina attack onset was performed exclusively in case of persisting clinical signs of myocardial ischemia or its equivalents.

In accordance with designated study aims, the patients were divided into 3 groups (Table 2). Group I included patients with blood flow restored within the first 3 hours from the disease onset (n = 1252). In a majority of patients from this group, blood flow in the IRA was restored as a result of prehospital thrombolysis or spontaneously. Group II (n = 2062) comprised patients with blood flow in the IRA restored within 3 to 6 hours from the disease onset. Patients with reperfusion achieved via endovascular procedure prevailed in this group. Group III (n = 465) comprised patients in whom reperfusion time exceeded 6 hours from the disease onset. This group consisted of patients who underwent reperfusion procedure due to persisting angina pain or other equivalents of myocardial ischemia.

As evident from Table 2, no significant differences in such parameters as age of patients,

Table 2. Main clinical and anamnestic characteristics in the studied groups of patients

Variable	Group I (n = 1252)	Group II (n = 2062)	Group III (n = 456)	p
Age (years)	58.2 ± 12.1	61.8 ± 10.5	59.1 ± 11.7	p = not significant (NS)
Male gender	991 (79.2%)	1678 (81.4%)	350 (76.7%)	p = NS
Smoking	893 (71.4%)	1406 (68.2%)	336 (73.7%)	p = NS
Arterial hypertension	660 (52.7%)	1198 (58.1%)	253 (55.5%)	p = NS
Hyperlipidemia	465 (37.1%)	740 (35.9%)	174 (38.1%)	p = NS
Diabetes mellitus	86 (6.9%)	151 (7.3%)	37 (8.2%)	p = NS
Duration of coronary heart disease (CHD) (months)	4.6 ± 1.8	5.2 ± 2.3	5.7 ± 2.1	p = NS
History of MI	206 (16.5%)	328 (15.9%)	82 (18.0%)	p = NS

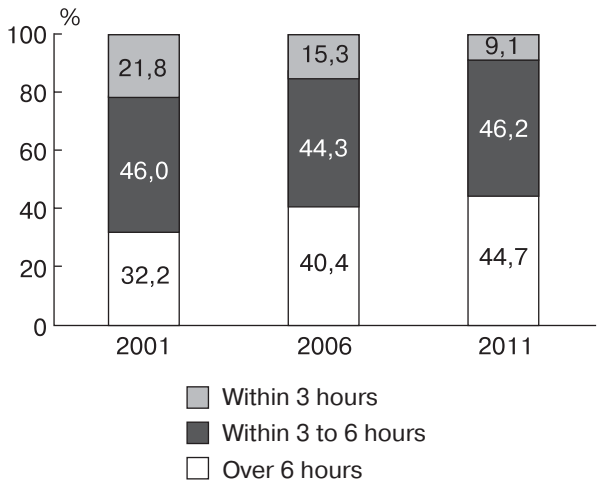

Figure 3. Proportion of AMI patients admitted in different terms over time.

gender, smoking, CHD duration, presence of arterial hypertension, hyperlipidemia, diabetes mellitus, history of MI were revealed. Therefore, patients from all three clinical groups were quite comparable in terms of main parameters.

When comparing pain-to-door values, it was revealed that over the follow-up period proportion of patients admitted within the first 3 hours from the disease onset continuously increased and by 2011 it exceeded 2001 values by one-third. The number of patients admitted within 3 to 6 hours almost did not change. Proportion of patients who were admitted later reduced approximately by half (Figure 3). Decreased time of patients' delivery to the in-patient department resulted from improved cooperation between emergency care services and medical preventive facilities and may be recognized as a positive event.

Analysis of in-patient treatment period parameters in AMI patients demonstrated that non-complicated course of the disease was observed in 1085 (86.6%) patients from Group I, 1654 (80.2%) patients from Group II and 286 (62.7%) patients from Group III, respectively. In patients with late reperfusion (Group III), acute left ventricular failure (cardiac asthma, pulmonary edema, cardiogenic shock) was observed significantly more often (17.1%) than in patients with reperfusion within 6 hours (7.4% and 4.1% in Groups II and I, respectively) ($p < 0.01$). Groups also differed in a number of patients with low ejection fraction of the left ventricle (LV). There were 21.5%, 14.4% and 9.6% of such patients in Groups III, II and I, respectively ($p < 0.01$). Groups III, II and I also significantly differed by the incidence of paroxysmal atrial fibrillation (12.2%, 7.8% and 4.2%, respectively ($p < 0.01$)). The groups significantly differed by the incidence of II–III degree AV-block. These complications were observed in 1.1%, 2.4% and 4.3% of such patients in Groups I, II and III, respectively (I–II $p < 0.05$; I–III $p < 0.01$; II–III $p < 0.05$). Mortality rate was 1.2%, 2.5% and 5.3% in Groups I, II and III, respectively (I–II $p < 0.05$; I–III $p < 0.01$; II–III $p < 0.01$) (Table 3). No significant difference in ventricular fibrillation rate was revealed between the groups; however, in Group I and II the cases of early primary ventricular fibrillations, apparently of reperfusion nature, significantly prevailed, while secondary VF with severe myocardial failure were significantly more often registered in Group III (Table 3 and 4).

Correlation analysis revealed statistically significant inverse relationship between pain-to-balloon parameter and non-complicated AMI course ($r = –0.45$; $p = 0.0074$). Statistically significant direct relationship between pain-to-balloon parameter and the rate of acute left ventricular failure was registered ($r = 0.46$; $p = 0.0086$). The same direct relationship was observed between pain-to-balloon parameter and the following parameters: LV EF < 40% in patients with primary anterior AMI ($r = 0.49$; $p = 0.0094$); the incidence of paroxysmal atrial fibrillation ($r = 0.41$; $p = 0.008$); the rate of degree II–III AV-block ($r = 0.49$; $p = 0.0094$); mortality ($r = 0.55$; $p = 0.0082$).

When analyzing obtained results, a group of AMI patients with effective prehospital thrombolysis and successful EVP (T + E) ($n = 503$) was identified separately. A group of patients who only underwent endovascular myocardial reperfusion within the first 6 hours from the disease onset was used for comparative analysis ($n = 2811$). Comparative analysis of serious complications in these two patient groups was conducted (Table 5).

In patients from T + E group, acute left ventricular failure occurred significantly more rarely (3.7%) than in control group patients (6.5%) ($p < 0.05$). Patients with ejection fraction lower than 40% were registered significantly more rarely in the studied group as compared to the control group (7.3% and 13.5%, respectively, $p < 0.01$). Meanwhile, it should be noted that rhythm disturbances such as ventricular fibrillation in this group were observed significantly more often than in the control group (8.1% and 5.4%, respectively, $p < 0.05$). Although paroxysmal atrial fibrillation, vice versa, was more often registered in the control group (6.8% and 4.2%, respectively, $p < 0.05$). Mortality and the

Table 3. Clinical and functional status of patients at the in-hospital stage

Variable	Group I (n = 1252)	Group II (n = 2062)	Group III (n = 456)	$p_{I–II}$	$p_{I–III}$	$p_{II–III}$
Non-complicated course	1085 (86.6%)	1654 (80.2%)	286 (62.7%)	<0.01	<0.01	<0.01
Killip II–IV acute left ventricular failure	51 (4.1%)	152 (7.4%)	78 (17.1%)	<0.01	<0.01	<0.01
Ejection fraction (EF) < 40% in patients with anterior AMI	120 (9.6%)	297 (14.4%)	98 (21.5%)	<0.01	<0.01	<0.01
Ventricular fibrillation	73 (5.8%)	122 (5.9%)	29 (6.3%)	NS	NS	NS
Paroxysmal atrial fibrillation	53 (4.2%)	161 (7.8%)	55 (12.2%)	<0.01	<0.01	<0.01
Degree II–III AV-block	14 (1.1%)	49 (2.4%)	19 (4.3%)	<0.05	<0.01	<0.05
Overall mortality	15 (1.2%)	52 (2.5%)	24 (5.3%)	<0.05	<0.01	<0.01

Table 4. The rate of ventricular fibrillation (VF) in the studied groups of patients

Variable	Group I (n = 1252)	Group II (n = 2062)	Group III (n = 456)	$p_{I–II}$	$p_{I–III}$	$p_{II–III}$
VF	73 (5.8%)	122 (5.9%)	29 (6.3%)	NS	NS	NS
Primary VF	59 (4.7%)	81 (3.9%)	5 (1.1%)	NS	<0.01	<0.05
Secondary VF	14 (1.1%)	41 (2.0%)	24 (5.2%)	NS	<0.01	<0.01

Table 5. The rate of serious clinical complications and mortality rate in two studied groups of patients: a) effective thrombolysis and successful endovascular procedure; b) successful endovascular procedure alone

Variable	Group of AMI patients:		p
	a) effective TLT + successful EVP (n = 503)	b) successful EVP within 6 hours (n = 2811)	
Killip II–IV acute left ventricular failure	19 (3.7%)	184 (6.5%)	<0.05
EF < 40% in patients with anterior AMI	37 (7.3%)	380 (13.5%)	<0.01
Ventricular fibrillation	41 (8.1%)	154 (5.4%)	<0.05
A. Primary VF	37 (7.3%)	103 (3.6%)	<0.01
B. Secondary VF	4 (0.8%)	51 (1.8%)	NS
Paroxysmal atrial fibrillation	21 (4.2%)	193 (6.8%)	<0.05
Degree II–III AV-block	4 (0.8%)	59 (2.1%)	NS
Overall mortality	6 (1.2%)	61 (2.2%)	NS

incidence of degree II–III AV-block were slightly lower in T + E group; however, no significant difference was revealed. Thus, the group of patients with T + E had better results regarding a number of complications characterizing clinical severity of AMI patients. However, as we already reported, episodes of primary ventricular fibrillation occurred significantly more often at the prehospital and immediate in-hospital stages in this group of patients. Taking into consideration that these rhythm disturbances were reported mainly during systemic thrombolysis, it may be suggested that myocardial reperfusion served as possible triggering mechanism (so called reperfusion arrhythmia) (Table 5).

According to the protocol adopted in the Moscow City Center of Interventional Cardioangiology, all AMI patients who underwent endovascular and pharmacological myocardial reperfusion during an acute stage of disease were invited for control examination in 6 months. Repeated examination in the in-patient department, including selective coronary angiography (CAG) and left ventriculography (VG) were performed in 935 (74.7%) patients from Group I, in 1503 (72.9%) patients from Group II and in 343 (75.2%) patients from Group III. Some patients refused from hospitalization due to feeling of well-being, absence of angina symptoms or circulatory failure. Information about their condition was obtained with the help of Seattle Angina Questionnaire for CHD patients and Minnesota Living with Heart Failure Questionnaire (MLHFQ). In total, information was obtained from 1158 (92.5%) patients of Group I, 1938 (93.9%) patients of Group II and 426 (93.4%) patients of Group III. The terms of complete control examination after endovascular procedure on average were 8.5 ± 1.1 months. It was 8.4 ± 1.2 months in the first group, 8.6 ± 1.1 months in the second group, and 8.5 ± 1.1 months in the third group; the difference was statistically insignificant ($p > 0.05$). Thus, during the long-term period information

Table 6. Results of examining the patients from the studied groups in the long-term period

Parameters	Group I (n = 1252)	Group II (n = 2062)	Group III (n = 456)	$p_{I–II}$	$p_{I–III}$	$p_{II–III}$
Information received	1158 (92.5%)	1938 (93.9%)	426 (93.4%)	NS	NS	NS
Complete examination	935 (74.7%)	1503 (72.9%)	343 (75.2%)	NS	NS	NS
Clinical presentation of angina	227 (19.5%)	411 (21.2%)	102 (23.9%)	NS	NS	NS
Restenosis/ reocclusion of the IRA	210 (16.8%)	385 (18.7%)	82 (17.9%)	NS	NS	NS
Repeated myocardial infarction	27 (2.3%)	43 (2.2%)	14 (3.3%)	NS	NS	NS
Cardiac failure (NYHA II-IV)	14 (1.2%)	91 (4.7%)	65 (15.2%)	<0.01	<0.01	<0.01
Mortality (3 months)	15 (1.2%)	58 (2.8%)	29 (6.3%)	<0.01	<0.01	<0.01
Mortality (8 months)	18 (1.4%)	77 (3.7%)	41 (9.0%)	<0.01	<0.01	<0.01

Table 7. LV ejection fraction values during long-term follow-up in the studied groups of patients over time

Variable	Group I (n = 935)	Group II (n = 1503)	Group III (n = 456)	$p_{I–III}$
EF before EVP (%)	53.6 ± 11.4	50.3 ± 9.7	46.6 ± 10.1	<0.05
ΔEF (%)	6.4 ± 2.9	2.1 ± 1.4	–2.6 ± 1.2	<0.05

about the presence of angina symptoms, cardiac failure, repeated infarctions was obtained from 3522 (93.4%) patients. Examination results are presented in Table 6.

Patients' clinical condition and treatment results were assessed in the long-term follow-up according to the following criteria: presence of angina symptoms, cardiac failure (NYHA II–IV), repeated MI, mortality, state of IRA. Comparative analysis of dynamic parameters (left ventricular ejection fraction, physical load tolerance) was conducted.

As is evident from Table 6, groups did not significantly differ in number of myocardial infarctions during the long-term follow-up. Also, differences between groups in the incidence of angina in patients during the long-term follow-up turned out to be insignificant ($p > 0.05$). Recurrence of angina was mainly associated with impaired myocardial vascularization as a result of in-stent stenoses of the coronary arteries. Studied groups had no significant differences in the incidence of restenoses and reocclusions. Circulatory failure was significantly more often observed in Group III (15.2%) than in Group II (4.7%) and I (1.2%) ($p < 0.01$). Mortality rate in 8 months was significantly higher in Group III (9%) than in Group II (3.7%) and I (1.4%). Differences between all studied groups were significant ($p < 0.01$) (Figure 4).

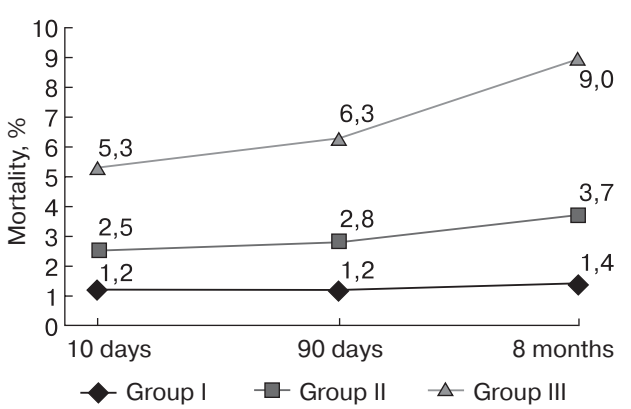

Figure 4. In-hospital and mid-term mortality in the studied groups of patients

The study demonstrated that the most positive change in the left ventricular function over time was observed in Group I where increase of LV EF was 6.4 ± 2.9%; EF increase, however to a lesser degree, was observed in Group II (2.1 ± 1.4%). Meanwhile, negative changes over time were registered in Group III where LV EF decreased as compared to baseline values (–2.6 ± 1.2%) (Table 7).

In order to determine reserve capacity of the coronary blood flow, the patients underwent a stress test. In Groups I and II, negative stress test was observed in 78.0% and 73.6% of patients, respectively, while in Group III this parameter was lower than in two other groups and was on average 61.3% (I–II $p < 0.05$; I–III $p < 0.01$; II–III $p < 0.01$) (Figure 5).

The groups differed also in physical load tolerance values (Figure 6). The level of load was on average 78.9 ± 11.2 W in Group I, 72.6 ± 12.7 W in Group II and 51.6 ± 10.1 W in Group III. As is evident from Table 8, the level of load in Group I and II was significantly higher than in Group III (I–II $p < 0.01$; I–III $p < 0.05$).

It should also be noted that total medium and high physical load tolerance was registered in 78% of patients from Group I, in 68.3% from Group II, and only in 47.5% of patients from Group III. Thus, in the first two groups the

Table 8. Capacity of achieved load in the long-term follow-up in the studied groups of patients

Variable	Group I (n = 935)	Group II (n = 1503)	Group III (n = 456)	$p_{I–III}$	p_{II-III}
Mean capacity of achieved load (W)	78.9 ± 11.2	69.6 ± 12.7	51.6 ± 10.1	<0.01	<0.05

Table 9. Main clinical and functional data from the studied groups of patients during the long-term follow-up

Parameters	Group of AMI patients + effective TLT + successful EVP (n = 503)	Group of AMI patients + successful EVP within 6 hours (control group) (n = 2811)	p
Information received	459 (91.2%)	2603 (92.6%)	NS
Complete examination	355 (70.6%)	2057 (73.2%)	NS
Clinical presentation of angina	84 (18.3%)	502 (19.3%)	NS
Repeated myocardial infarction	9 (1.8%)	54 (2.1%)	NS
NYHA II-IV cardiac failure	4 (0.9%)	98 (3.7%)	<0.01
Mortality (8 months)	7 (1.5%)	85 (3.3%)	<0.05

patients with high and medium physical load tolerance comprised the majority, while in Group III the patients with low tolerance significantly prevailed (I–III $p < 0.05$; II–III $p < 0.05$).

Patients with T + E (n = 503) in the long-term follow-up were studied as a separate group. Assessment was conducted according to criteria specified above. Clinical and functional data of patients who underwent only endovascular procedure within the first six hours from the onset of angina attack without preceding thrombolysis (n = 2811) were used for comparison (control). In 8 months, the information from 459 (91.2%) patients of T + E group and from 2603 (92.6%) of control patients was received. 355 (70.6%) patients from T + E group and 2057 (73.2%) patients from the control group underwent complete repeated examination (Table 9). Conducted study demonstrated that mortality rate in T + E group in 8 months was only 1.5%, whereas in the control group this value was 3.3%, the difference was significant ($p < 0.05$). Clinical manifestations of Class II–IV (NYHA) circulatory failure were significantly more rarely observed in T + E group (0.9%) than in the control group (3.7%), ($p < 0.01$).

Discussion of the results

Providing medical care to the patients with acute conditions as fast as possible is one of the important problems of emergency care services which is not completely solved. This refers to the majority of diseases including cardiovascular diseases. Timing of providing medical care to patients appears to be crucial in acute myocardial infarction. This circumstance became especially important after implementing methods of urgent myocardial revascular-

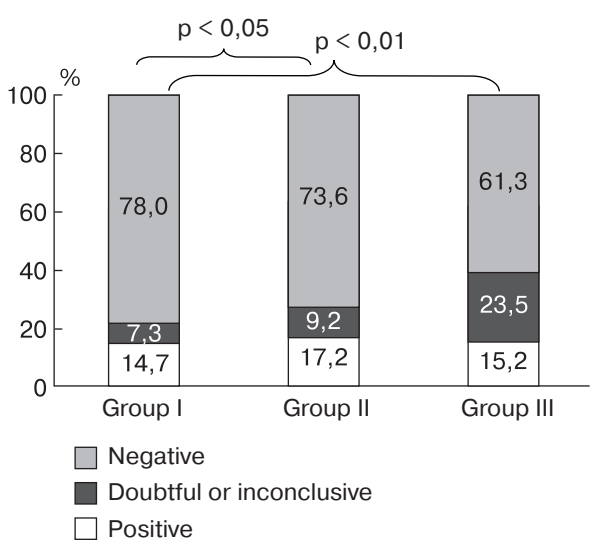

Figure 5. Results of stress tests in patients from the studied groups in the long-term follow-up.

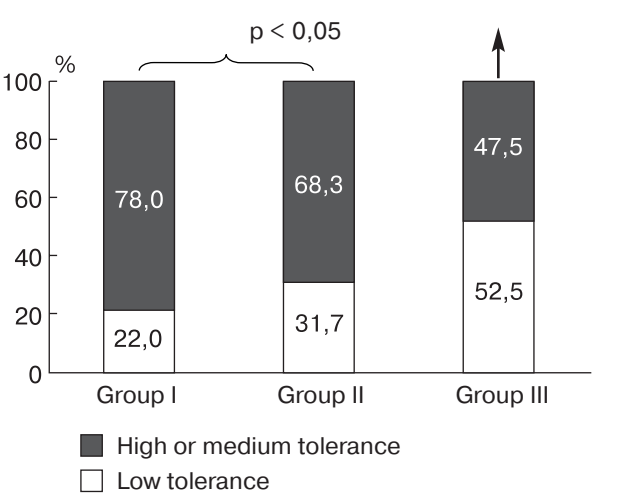

Figure 6. Physical load tolerance in the long-term follow-up in studied groups.

ization into the clinical practice. Today it is no longer a secret that the earlier blood supply of the infarct and peri-infarct zone is restored, the smaller is myocardial damage, and therefore, immediate and long-term prognosis in AMI patients improves (25, 28). Hence, physicians attach great importance to optimization of organizational measures on providing emergency care to AMI patients at all stages of the disease and on informing population about necessary actions that have to be undertaken if the disease symptoms occur. In particular, emphasis is laid on informing the population about the first treatment measures which patients can perform on their own, as well as on the need to immediately call an ambulance (17, 21, 22, 29). Effective coordination of actions between emergency medical services and in-patient departments that can help maximally reduce the time of providing first aid to a patient and of his/her delivery to the in-hospital department is also important.

Moscow City Center of Interventional Cardioangiology has a great experience of organizational and treatment measures regarding AMI patients. Together with Moscow Emergency Medical Service with the assistance of Moscow Healthcare Department, based on the interdisciplinary systemic approach that ensures principles of interaction and succession in the work of emergency medical services and preventive medical facilities at different stages, we have initiated measures aimed at optimization and effectivization of providing care to the patients with acute myocardial infarction. They involved measures on maximal reduction of the time required for arrival of specialized ambulance units to the patient, as well as implementing medical measures at the prehospital stage aimed at myocardial reperfusion (prehospital systemic thrombolysis). Implementation of such approach in treatment of patients with acute coronary blood flow impairment only became possible thanks to the effective coordination between emergency medical care services with 24-hour services of emergency cardiology and radioendovascular departments of municipal preventive medical facilities. By optimizing pre-hospital treatment stage and improving interactions between emergency care services and Moscow City Center of Interventional Cardioangiology, we managed to implement prehospital systemic thrombolysis into the clinical practice and reduce the time of possible myocardial reperfusion in some patients approximately by 60 minutes as compared to values when reperfusion was performed in the in-patient settings (104 ± 7 minutes vs. 162 ± 15 minutes; p = 0.007) (1). Our study also demonstrated that due to a wide use of prehospital thrombolysis, the number of AMI patients with prehospital thrombolysis delivered to the Moscow City Center of Interventional Cardioangiology annually increased, and by 2011 it constituted 45% out of all admitted AMI patients.

In 11 years we managed to reduce the time required for delivery of AMI patients to the in-hospital department (so called pain-to-door time) by 30 minutes which is rather significant in the settings of annually increasing Moscow traffic. Over the follow-up period, door-to-balloon interval also decreased by 17 minutes. As a result of reduction of these two intervals and faster delivery of patients to the in-patient department, the number of patients who underwent endovascular treatment within 3 hours from AMI onset significantly increased. We believe that due to exactly these measures (in particular, as a result of widespread implementation of prehospital thrombolysis) we managed to decrease in-hospital mortality rate in the Center from 4.6% to 1.2% with average value of 2.3% throughout the entire follow-up period. Conducted study revealed direct correlation between the time from the onset of angina status before reperfusion, on one hand, and in-hospital mortality, on the other hand. The same correlation was observed between the above-specified parameter and the incidence of threatening complications. Obtained data once more confirm the importance of early myocardial reperfusion in order to improve prognosis in AMI patients. This can be proved by the fact that the lowest rate of mortality and severe complications was observed in the group of patients who underwent reperfusion within the first three hours from the disease onset. Analysis inside this group convincingly proved that the lowest mortality rate was observed in patients who underwent successful systemic thrombolysis at the prehospital stage followed by successful angioplasty of the IRA, urgently performed in the in-patient department. The largest increase of LV ejection fraction (6.4 ± 2.9%) and the highest values of achieved load capacity during bicycle ergometry (78.9 ± 11.2 W) were observed in the same group of patients in the mid-term period as compared to the patients from other groups. Data that we received correspond with the study results of J. Blankenship et al. (16) who

investigated clinical results of 676 AMI patients including in-patient and annual mortality depending on the time from the onset of angina attack until reperfusion. It turned out that throughout the whole follow-up period, i.e. from 2004 through 2007 inclusive, pain-to-door interval almost did not change, while door-to-balloon interval decreased by more than half; the authors associate it with decrease in annual mortality rate from 10.1% to 4.4%. Relation between the disease outcome and the time when reperfusion was conducted was also registered in the study HORIZONS-AMI (17).

As we already noted above, the lowest in-hospital mortality rate was observed in AMI patients with effective prehospital thrombolysis and successful EVP. Non-complicated clinical course and the best values of left ventricular functional state were observed more often in the same patients. However, it should be noted that ventricular rhythm disturbances, including ventricular fibrillation, were observed in this group of patients significantly more often than in other studied groups. This is consistent with data from some foreign studies where the incidence of ventricular arrhythmias accompanying *ST*-segment elevation AMI increased during fibrinolytic therapy which, according to the authors, was associated with reperfusion metabolic processes in the myocardium (23, 24, 33, 35). Most likely, it would be wrong to unambiguously assess predictive value of these reperfusion ventricular arrhythmias. If ventricular arrhythmias appear at the late stages of myocardial revascularization, they can adversely affect further prognosis, as significant reperfusion injury caused by exposure to products of myocytolysis develops simultaneously with ischemic necrosis. In other cases, including the early terms of myocardial reperfusion, occurrence of reperfusion arrhythmias does not significantly affect the immediate and long-term prognosis in AMI patients (30–36). Our study can serve as a proof to this fact.

As a result of conducted study, we made a few conclusions which clearly come out of the study results. The first and the most important conclusion consists in the fact that myocardial reperfusion in STEMI patients beneficially affects the immediate and mid-term disease prognosis regardless of whether reperfusion was achieved pharmacologically or via the endovascular procedure. Secondly, prehospital systemic thrombolysis makes it possible to achieve myocardial reperfusion significantly earlier than after endovascular procedure in the in-patient settings. Therefore, in those cases where delivery of AMI patient to the in-patient department may be delayed because of a serious traffic jam or for some other reasons, we consider it reasonable to perform systemic thrombolysis in a patient with subsequent coronary angiography and possible angioplasty procedure on the IRA in the in-patient settings. This allows us to buy time for myocardial reperfusion with further correction of the IRA in the in-patient department, if necessary. In no case should pharmacological and endovascular myocardial reperfusion be considered as alternative treatment methods; cardiologists must operate those mutually complementary methods at different stages of treatment. The study that we conducted convincingly proved that the best immediate and mid-term prognosis was observed in patients who underwent successful prehospital thrombolysis followed by angioplasty of the IRA in the in-patient settings. All that has been said, of course, can be primarily applied to those cases when in-patient department is not “few steps” away and it is expected that some time required for delivery of the patient to the hospital will be lost. Thirdly, it is necessary to improve the emergency care service and optimize providing of pre-hospital care to AMI patients, including the possibility of prehospital systemic thrombolysis as indicated and, of course, in the absence of contraindications. Also, we consider it extremely important to arrange absolute mutual understanding and close contacts between emergency care services and preventive medical facilities involved in emergency cardiology. Only such contact will allow us to maximally optimize treatment of AMI patients and to reduce time from the onset of angina attack till conduction of necessary medical and diagnostic procedures in a patient. And of course, the role of emergency care is priceless regarding hospitalization of STEMI patients into the closest in-patient departments with 24-hour services of emergency cardiology and radiosurgical methods of treatment.

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Retrograde Approaches for Recanalization of Complex Infrainguinal Arterial Occlusive Disease

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The results of retrograde transpopliteal and tibial approaches for complex infrainguinal arterial occlusive disease are analyzed. The clinical report includes 30 patients with long femoropopliteal and tibial occlusions, who had retrograde recanalization after failed antegrade attempt. Technique of transpopliteal and tibial approaches, immediate results, complications, and reasons for technical failures are described.
Key words: *endovascular intervention, retrograde approach.*

Objective. To determine the efficacy of retrograde approaches for recanalization of chronic infrainguinal arterial occlusive disease.

Material and methods. 30 patients with long occlusions of infrainguinal arteries underwent endovascular interventions (EI) using retrograde approaches from 2011 till 2012. Failed attempt to perform antegrade recanalization of occluded arteries was an indication for retrograde approach. Mean lengths of femoropopliteal and crural occlusions were 19 ± 8 cm and 17 ± 14 cm, respectively. Group 1 included 16 patients with affected superficial femoral artery (SFA) and proximal part of the popliteal artery (PA), who had retrograde approach via SFA or PA (14 cases) and the upper third of the anterior tibial artery (ATA) (2 cases). Group 2 included 14 patients with affected distal part of PA and tibial arteries who had approach via the upper third of ATA (2 cases) and distal parts of the tibial arteries (12 cases).

Results. In Group 1, EI were technically successful in 81% of cases. 4 patients from this group (25%) had balloon angioplasty followed by additional stenting of SFA. Three EI at this arterial segment failed (19%). In Group 2, technical success of EI was achieved in 12 patients (86%). Five patients (36%) had balloon angioplasty followed by additional stenting of the crural arteries. In 5 cases (17%), intraluminal arterial space was not achieved using both antegrade and retrograde approach, and two-balloon technique was used. There were no complications related to retrograde puncture of the popliteal and tibial arteries. A total number of complications related to retrograde recanalization was 3 (10%) in two groups.

Conclusions. Retrograde approach is an alternative method for lower limb revascularization after failed antegrade recanalization, which significantly increases efficacy of EI in infrainguinal arterial occlusive disease.

Lower limb revascularization in patients with complex infrainguinal arterial occlusive disease is a difficult problem in vascular and endovascular surgery. Currently, endovascular interventions (EI) are widely used for lower limb revascularization. EI success achieves 100% when standard antegrade approach is used for simple infrainguinal arterial disease. In case of long occlusions, the EI results are significantly worse. When standard antegrade approach is used for recanalization of long femoropopliteal (FP) and crural occlusions, failure rate is up to 25% and 40%, respectively (1, 2). The reasons for EI failures related to antegrade approach are the impossibility to enter postocclusion patent arterial lumen when subintimal angioplasty is used; impossibility to penetrate long calcified occlusions using the wire and supportive catheter; arterial perforation when attempting to penetrate occlusion; large collaterals originating from the occluded artery stump which do not allow the wire and catheter to enter occlusion. In these cases, retrograde approaches may be alternatives with >90% success rate after failed antegrade recanalization attempts (3,4). The objective of the study was to determine the efficacy of retrograde approaches for recanalization of chronic infrainguinal occlusions.

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Manuscript received on May 22, 2013
Accepted for publication on June 17, 2013

Material and methods

234 infrainguinal arterial EI for lower limb revascularization were performed in our Institute from 2011 till 2012. The second retrograde approach was additionally used in 30 patients (13%) after failed attempts to recanalize the occluded arteries using antegrade approach. Table 1 presents demographics and clinical characteristics of patients who had retrograde approach. The primary indication for retrograde approach to be used was arterial patency distal to the occlusion. Table 2 shows lesion localization, distribution of retrograde approaches and arterial segments at which EI were performed, and EI technical success. FP occlusion length varied from 7 up to 39 cm (mean = 19 ± 8 cm). According to TASC II, FP lesions were classified as follows: type B – 28%, type C – 33%, and type D – 39%. Tibial occlusion length varied from 5 to 35 cm (mean = 17 ± 14 cm). The patients were assigned into two groups. Group 1 included 16 patients with affected superficial femoral artery (SFA) and proximal part of the popliteal artery (PA) who had retrograde approach via SFA or PA (14 cases) and the upper third of the anterior tibial artery (ATA) (2 cases). Group 2 included 14 patients with affected distal part of PA and tibial arteries who had approaches via the upper third of ATA (2 cases) and distal parts of the tibial arteries (12 cases).

Retrograde technique

If retrograde approach was used, femoral contralateral or ipsilateral antegrade catheterization of the common femoral artery (CFA) was initially performed in all cases. If antegrade revascularization failed and occluded arteries of FP segment were to be recanalized, SFA or PA retrograde puncture with 18 G needle was performed and 6F introducer sheath was inserted. SFA or PA was punctured using roadmap function or under X-ray control when contrast media passed through the introducer sheath placed in CFA. If SFA was punctured at the lower third, a patient was in supine position, his/her knee was mildly flexed and rotated outside; if PA was punctured, a patient was in prone position. To penetrate FP occlusion, a hard hydrophilic 0.035 wire (Radifocus, Terumo) was used and supported with balloon catheter or vertebral diagnostic catheter. When the wire and catheter entered true SFA lumen above the occlusion, it was captured and externalized through the upper introducer sheath using the diagnostic catheter JR 6F. Then balloon catheter was passed antegradely over this wire, and EI was performed. If true lumen was

Table 1. Clinical and demographic characteristics of patients

Number of patients	30
Mean age, years	63.4 ± 8.3
Males / Females	17 (57%)/13 (43%)
Diabetes mellitus	19 (63%)
Smoking	15 (50%)
Chronic renal insufficiency	2 (7%)
Arterial hypertension	20 (67%)
Previous myocardial infarction or stroke	11 (37%)
Grade 2 ischemia	3 (10%)
Grade 3 ischemia	4 (13%)
Grade 4 ischemia	23 (77%)

Table 2. Lesion localization, retrograde approaches, and EI technical success

	Group 1 (n = 16)	Group 2 (n = 14)
Localization of arterial lesions	SFA + proximal PA (16)	Distal PA (2) Distal PA + ATA (2) Distal PA+Tibial-peroneal trunk (TPT) +PTA (1) ATA (5) PTA (1) PTA + TPT (1) PTA + FA (1) TPT + FA (1)
Retrograde approach	SFA (2), PA (12), Upper third of ATA (2)	ATA (9), PTA (4), FA (1)
EI technical success	81%	86%

not achieved using both antegrade and retrograde approaches, two-balloon technique was used. These balloons were entered antegradely and retrogradely until contact and then were inflated simultaneously (5). This technique disrupts the membrane between two subintimal canals and makes it possible for one of the wires to enter true lumen antegradely or retrogradely.

4-cm 21 G needles were used for retrograde puncture of crural arteries. ATA was punctured at the anterior view at the level of the back of the foot, posterior tibial artery (PTA) was punctured at the lateral view at the level of the ankle, fibular artery (FA) was punctured at the oblique view above the ankle under X-ray control at the moment when the contrast agent passed through it. If ATA was punctured at the upper third of the lower leg, 7-cm 21 G needle was used. Then, there were two intervention options: first option included no introducer sheath, the second option used 4F sheath (5). If the first option was used, 300 cm 0.014 wire (PT 2, Boston Scientific) was passed into the artery as far as possible, over which a low-profile balloon catheter (Amphirion Deep, Invatec-Medtronic) was passed retrogradely as a support. If occlusion could not be passed using 0.014 wire, the latter was replaced with harder 300 cm 0.018 wire (Glidewire Advantage, Terumo) with the supportive balloon catheter (Pacific Extreme, Invatec-Medtronic). The wire and catheter were moved above the occlusion into the arterial lumen patent from above, where the end of the wire was captured and externalized using the diagnostic catheter Judkins right (Fig. 4d) (4). Further, the balloon catheter was removed and re-introduced into the artery antegradely through the sheath in CFA and moved down to the free distal arterial lumen. After that, the wire was also removed and re-entered through the catheter antegradely with the soft tip down to the free arterial segment, then balloon dilatation of the occluded arterial segment was performed. During the second option with sheath, 4 Fr introducer sheath (Radifocus, Terumo) was inserted after artery puncture and the wire insertion into the tibial artery; further, EI was performed in accordance with the technique described above. Prior to tibial artery puncture, heparin 7,500–10,000 U and nitroglycerin 200 μg were given intraarterially. If residual stenosis exceeded 30% or there was an obstructive dissection, additional stenting was used. Hemostasis was achieved via inflation of the balloon catheter at the puncture site or via external manual compression for 5–10 minutes.

Results

The retrograde punctures were successful in all patients from Group 1. PA was punctured in the vast majority of cases (Fig. 1). SFA was punctured in 2 patients, one of them had puncture of in-stent occlusion because the wire could not be passed antegradely in the in-stent occluded segment (Fig. 2). Two patients were punctured at the upper third of ATA due to this fact that the dissection was spread antegradely to ATA orifice during recanalization. EI technical success in this group was 81%. In 4 cases when after occlusion passage the intraluminal arterial space was not achieved using both antegrade and retrograde approaches, two-balloon technique was used which was successful in 3 patients. Four patients from this group (25%) had additional SFA stenting using nitinol self-expanding stents (Smart, Cordis or Misago, Terumo). 3 EI at this arterial segment failed (19%). All FP lesions with failed interventions were type C and D by TASC II classification and their mean occlusion length was 27 cm. In two cases, true arterial lumen was not achieved when using both antegrade and retrograde subintimal angioplasty. In one case, the reason for failed attempt was SFA perforation precluding further intervention. Since the occluded arterial part was perforated, there were no serious clinical consequences and additional interventions. These three patients with failed EI underwent elective femoral-popliteal bypass grafting.

The technical success of retrograde tibial puncture and EI was achieved in 12 patients (86%) from Group 2 (Fig. 3, 4). Two patients from this group had successful punctures of the upper third of ATA and recanalization of the distal part of PA (Fig. 5). In one case, two-balloon technique was successfully used to enter the true lumen. Five patients (36%) had additional stenting of crural arteries using balloon-expandable coronary stents. EI in two patients failed due to unsuccessful attempts to pass the wire and supportive catheter retrogradely through long calcified occlusions of ATA and PTA to the upper patent arterial segments. There were no complications related to retrograde PA and tibial puncture. The next morning, final angiography and US confirmed the absence of complications at the site of retrograde puncture. A total number of complications related to retrograde recanalization was 3 (10%) in two groups: 1 SFA perforation result-

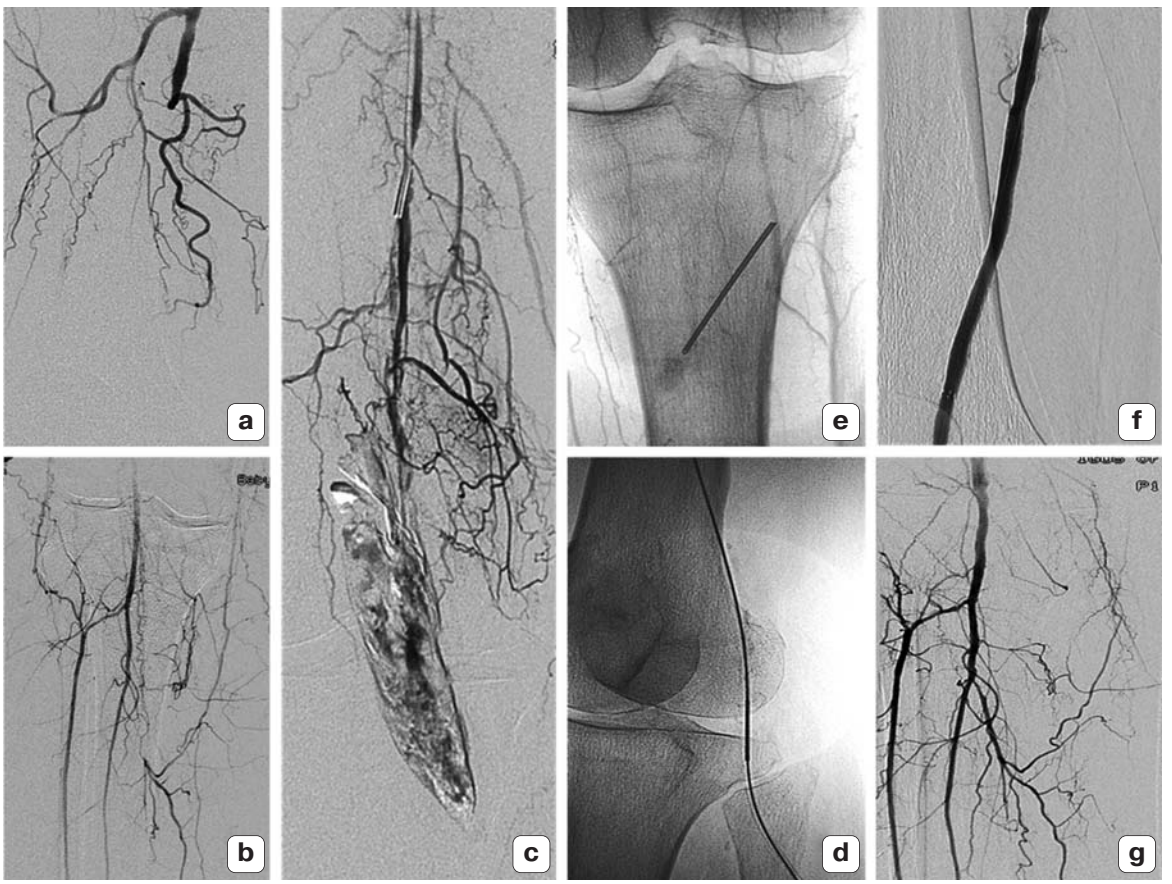

Figure 1. Occlusion of the lower third of SFA + proximal part of PA (a, b); PA perforation at attempted antegrade recanalization (c); PA retrograde puncture and catheterization (d, e); percutaneous balloon angioplasty (PBA) and stenting of the lower third of SFA + proximal part of PA (f, g).

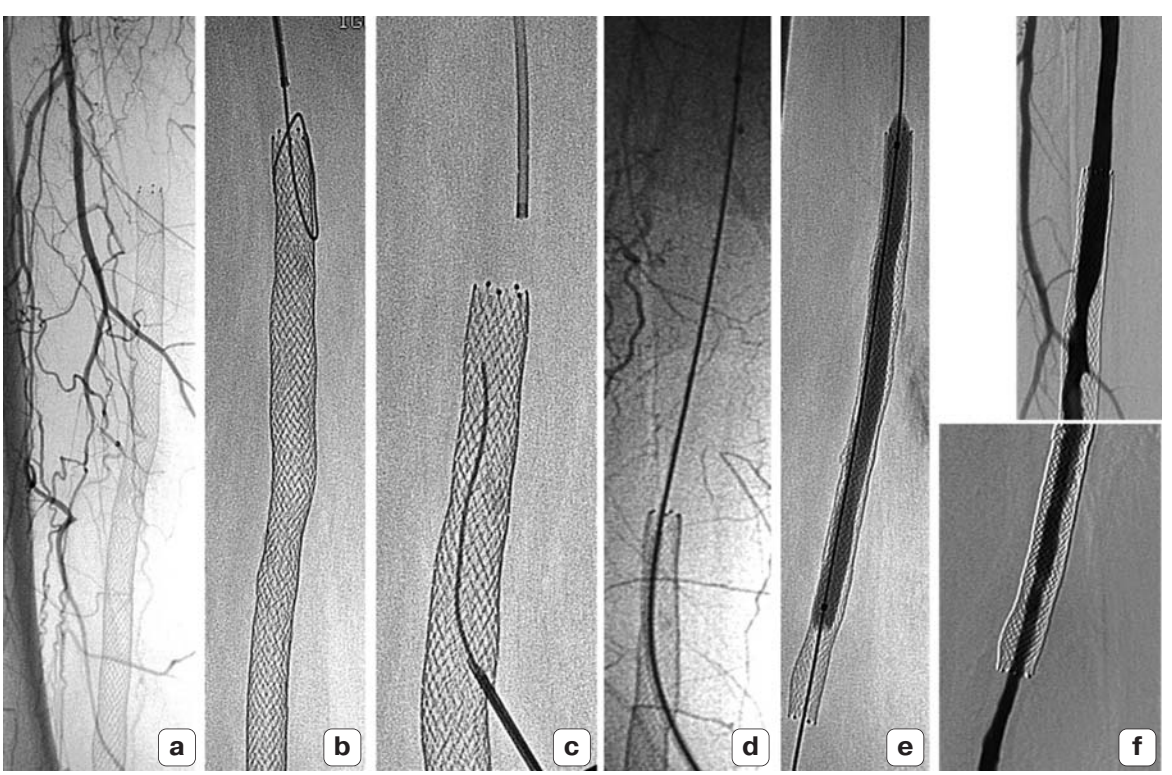

Figure 2. Re-occlusion after SFA stenting (a); failed attempt to pass the stent antegradely (b); puncture of the in-stent occlusion (c); retrograde wire passage through the occlusion (d); antegrade recanalization of the occlusion (e); outcome after balloon dilatation of the in-stent occlusion (f).

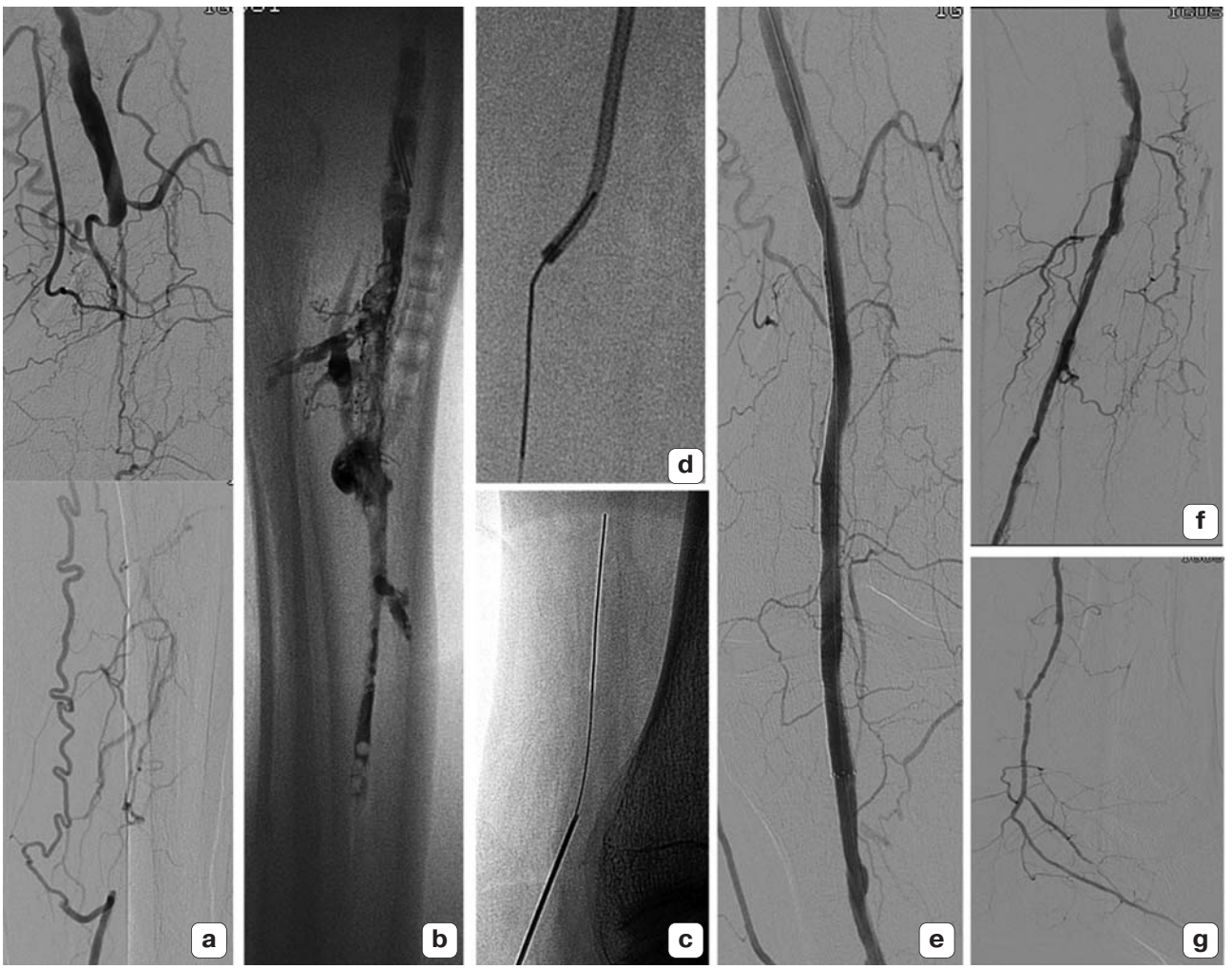

Figure 3. Occlusion of PA, TPT and upper third of PTA (a); TPT perforation and arteriovenous fistula (b); retrograde approach via PTA (c); wire externalization (d); outcome after PBA and stenting of PA, TPT, and PTA (e, f, g).

ed in intervention failure, 1 PA arteriovenous fistula was cured by long-term balloon tamponade, 1 PTA distal embolism resolved successfully using catheter-directed thrombolysis. After retrograde approach, there were no major amputations during in-hospital period.

Discussion

The main reason for EI failure in recanalization of SFA chronic occlusions is the impossibility to enter true arterial lumen below the occlusion. Such re-entry devices as Outback (Cordis) or Pioner (Medtronic) make it possible to enter true arterial lumen below the occlusion almost in 100% of cases. Unfortunately, these devices are expensive and intervention costs are quite high, thus limiting their wide application in the routine clinical practice. Retrograde approach via PA may be an alternative to re-entry devices. Retrograde PA puncture was first described by Tönnesen K.H. et al. in 1988 (6). The majority of interventionists consider the failed antegrade recanalization to be the main indication for retrograde transpopliteal approach. Moreover, indications for retrograde infrapopliteal approach in SFA occlusions may be SFA ostial or in-stent occlusions, large collaterals originating from the occluded artery stump, groin postoperative scars, and obesity (3). According to the standard technique, PA is punctured retrogradely after prone positioning; this extends intervention time, jeopardizes sterility and is often uncomfortable for patients especially those with heart failure or obesity. For patients with SFA occlusion not spreading to the Hunter's canal, the modified retrograde transpopliteal approach below the Hunter's canal is used to puncture at the medial lower third of the femur without proning the patient (7). We used successfully this approach in 5 cases (30%). It should be noted that passing the wire in the intralumenal arterial space via retrograde approach is not always possible. In such cases, two-balloon technique can be

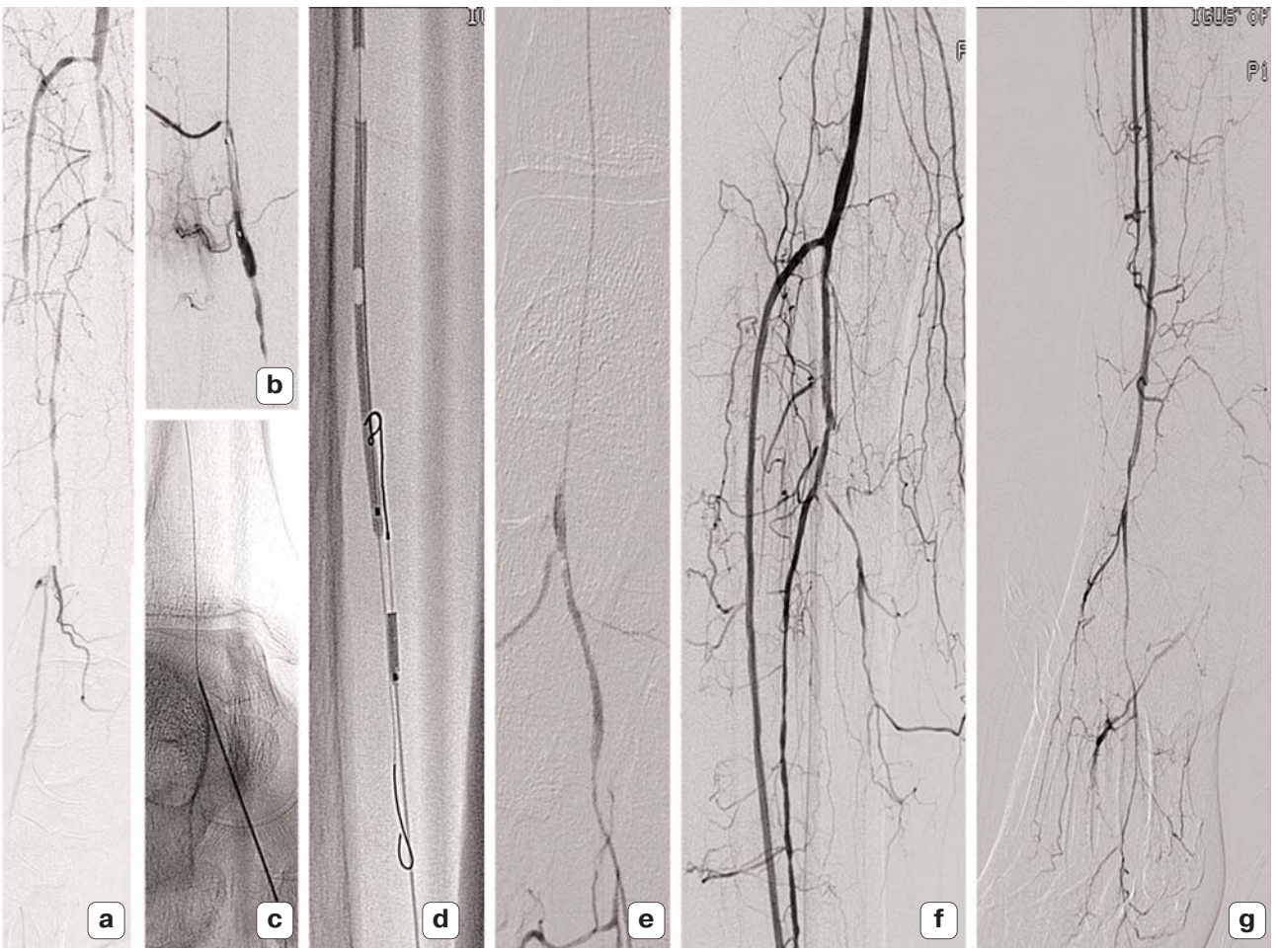

Figure 4. Occlusion of the middle and lower thirds of ATA, multiple stenoses of TPT and FA, whole PTA occlusion (a); failed attempt to pass ATA (b); retrograde approach through ATA (c); wires and balloon catheters inserted in ATA using two approaches by rendezvous technique (d); catheter placed in the dorsalis pedis artery (e) outcome after PBA of ATA, TPT, and FA (f, g).

used, which in our experience was successful in 3 out of 4 cases. EI technical success in FP segment using retrograde transpopliteal approach varies from 80 to 100% according to various authors (8–10). In our serial observations, EI were technically successful in 81% of cases, as consistent with the published data.

The issue of recanalization of chronic tibial occlusions is even more topical because the number of failed antegrade recanalizations in this arterial segment is significantly higher. To date, there are no re-entry devices intended for crural arteries. Therefore, retrograde revascularization is very important for increasing EI efficacy in tibial arterial occlusions. Although not all patients are eligible for retrograde tibial approach, distal segments of tibial arteries are sufficiently wide for puncture in 80–90% of patients (4). Retrograde approach via PTA was first described by Lyer S.S. et al. in 1990 (11). In the vast majority of cases, retrograde revascularization was performed in patients with critical lower limb ischemia. The indications for retrograde tibial approach were: impossibility to penetrate the occlusion using the wire, to enter the true arterial lumen below the occlusion, or arterial perforation preventing further intervention. In the majority of authors' opinion, the retrograde tibial approach may be warranted only after failure of previous intervention via the antegrade approach. We used the retrograde tibial approach in case of failed antegrade recanalization only. The efficacy of the retrograde tibial approach in complex occlusive tibial disease is up to 90% with 1-year limb salvage achieving about 70% (5, 12, 13). In our serial observations, the efficacy of EI using retrograde tibial approach was 86%; it does not significantly differ from the foreign data.

The mechanism of the superiority of the retrograde recanalization over the antegrade recanalization is not fully understood. The possible reason is that the distal part of occlusion contains less amount of fibrotic and calcified

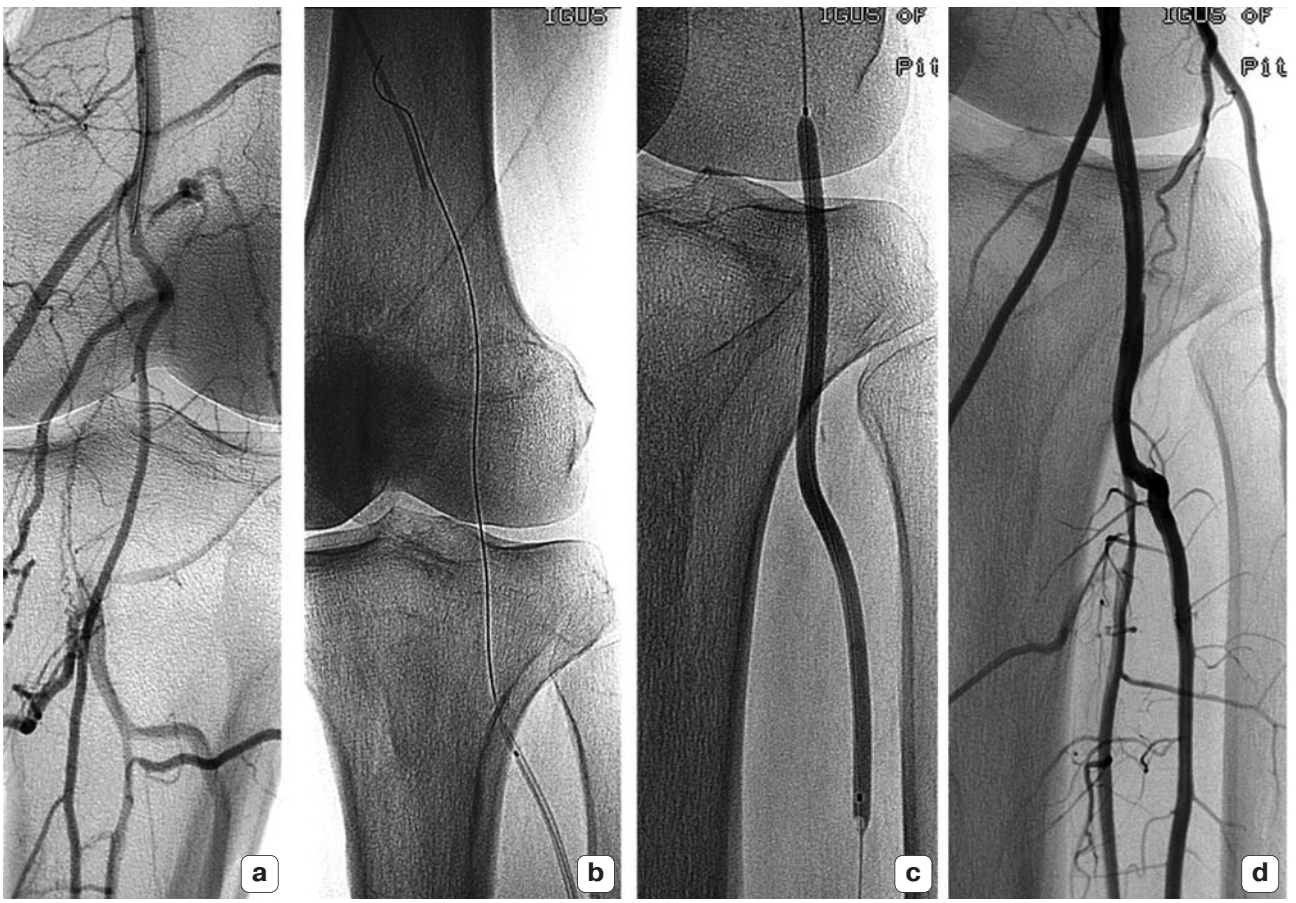

Figure 5. Occlusion of non-stumped PA (a); retrograde approach through the upper third of ATA (b); PA PBA (c); outcome after PA PBA (d).

tissue and, therefore, it's less dense compared to the proximal part. (14, 15). In the opinion of authors whose experience exceeds 300 interventions via retrograde approach, higher efficacy of the retrograde recanalization is determined by two factors. The first: the same lesion is subjected to the second recanalization attempt after the first one failed. The second: craniocaudal collaterals usually originate from the beginning of the occlusion, impeding maintenance of the direct passage of the wire antegradely because the wire enters collaterals easily. Therefore, retrograde passing helps to maintain intraluminal motion of the wire and facilitates its entry to the true arterial lumen above the occlusion (4).

Conclusion

Retrograde approach is safe and effective method for recanalization of chronic femoropopliteal and crural occlusions. Retrograde approach may be an alternative method for lower limb revascularization after failure of antegrade recanalization, increasing significantly EI efficacy in complex infrainguinal arterial occlusive disease.

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The Use of Intravascular Diagnostic Techniques for Coronary Bifurcation Lesions

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Endovascular correction of coronary artery bifurcation lesions is currently one of the most thrilling problems. Modern intravascular diagnostic techniques are considered to be an effective instrument in achieving optimal immediate and long-term results. The article analyzes immediate results of percutaneous coronary interventions in patients with coronary artery bifurcation lesions whose fractional flow reserve was measured and whose target lesions were examined by intravascular ultrasound. According to study results, modern methods of intravascular assessment should be actively used to achieve the best clinical results.

Key words: *coronary bifurcation lesions, intravascular ultrasound, fractional flow reserve.*

List of abbreviations:

CHD – coronary heart disease
LAD – left anterior descending artery
CA – circumflex artery
RCA – right coronary artery
OMB – obtuse marginal branch
PLB – posterolateral branch
DB – diagonal branch
IVUS – intravascular ultrasound
FFR – fractional flow reserve
QCA – quantitative coronary analysis
MB – main branch
SB – side branch

Treatment of patients with coronary heart disease (CHD) remains one of the most topical problems of the highest priority in the global and national healthcare. Russia holds a leading place in Europe for CHD morbidity and mortality (Bokeria L.A., 2010). Interventional cardiology is a dynamically developing field of medicine in treatment of CHD (Iosseliani D.G., 2011).

Implementation of intravascular diagnostic techniques into clinical practice added new coronary angiography data about the structure of atherosclerotic plaque, made it possible to more accurately judge about its quantitative parameters and functional importance (Gussenhoven W., 1991; Gould K., 1990; Mallery J., 1987; Nissen S., 1991; Pijls N., 1995; Tobis J., 1996; Yock P., 1988). Practical and clinical importance of intravascular ultrasound and fractional flow reserve measurement have already been investigated during the studies in patients with linear stenoses [AVID; FAME; MUSIC; OPTICUS; RESIST] (4). Results of these studies extended indications for their use, optimized the strategy of endovascular intervention and made it possible to develop new criteria for stenting assessment (Bellenger N., 2007; Koo B., 2005).There are only single works on the use of intravascular diagnostic methods during bifurcation stenting in the national literature (Ivanov V.A., 2008; Movsesyants M.Yu.; 2009, Demin V.V1., 2010). Therefore, it is topical and timely to study the results of using intravascular diagnostic methods during stenting of coronary artery bifurcation stenoses (1, 2).

Objective of the study is to investigate capabilities of intravascular ultrasound and fractional flow reserve measurement in complex diagnostics of coronary artery bifurcation stenoses, their effect on the choice of endovascular intervention tactics and clinical results of the treatment.

Study materials

During the period from 2009 till 2012, CHD patients with coronary artery stenoses were

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Manuscript received on April 16, 2013
Accepted for publication on May 13, 2013

studied in A.A. Vishnevsky 3rd Central Military Clinical Hospital of the Ministry of Defence of the Russian Federation on the basis of Diagnostic and Treatment Center of Interventional Radiology.

The studies were conducted in patients with functional class (FC) II-III exertional angina (according to Canadian Cardiovascular Society grading), with isolated bifurcation lesion of the LAD, CA or RCA (diameter of the side branch (DB, OMB, PLB) not less than 2.25 mm and the extent of atherosclerotic lesion in the orifice not more than 10 mm).

All patients were prescribed complex pharmacologic therapy including aspirin, statins, β-adrenoblockers, ACE inhibitors, hypolipidemic agents, short-term and long-term nitrates. Clopidogrel at a dose of 75 mg/day was prescribed 3–4 days prior to the surgery. Double desaggregant therapy was prescribed for at least 12 months.

Results of coronary angiography at various stages of endovascular procedure were supplemented with data of intravascular diagnostic methods. The choice of stent size and immediate result assessment of the stenting of the main branch (MB) of bifurcation stenting were performed based on data of intravascular ultrasound (IVUS). Angioplasty of the side branch (SB) orifice was conducted only if fractional flow reserve (FFR) was lower than 0.75 regardless of the degree of luminal narrowing. If FFR value was less than 0.75 at control measurement or in case of intimal dissection limiting the blood flow, the procedure was supplemented with SB orifice stenting (transformation into T-stenting). Immediate result was assessed by generally accepted angiographic and intravascular ultrasound criteria of optimal stent implantation. Post-dilation in stents was performed by high-pressure short balloon in case of neointimal stent implantation according to the results of control IVUS.

Coronary angiography was performed using digital angiographic complexes Allura FD 10 (Philips, Holland) and Innova 4100 (GE, USA) according to M. Judkins technique. Contrast medium (Visipaque-320, Omnipaque-300, Ultravist-370) was administered manually into the coronary artery (5–7 mL per each injection). The type of myocardial blood supply, evenness of the coronary artery contours and the rate of their filling with the contrast medium, as well as spatial relation between bifurcation branches were assessed visually. Quantitative analysis of stenoses was performed using integrated computer program of quantitative coronary analysis (QCA). 50% or more narrowing of arterial luminal diameter in the most informative projection served as criterion for hemodynamic significance of stenosis.

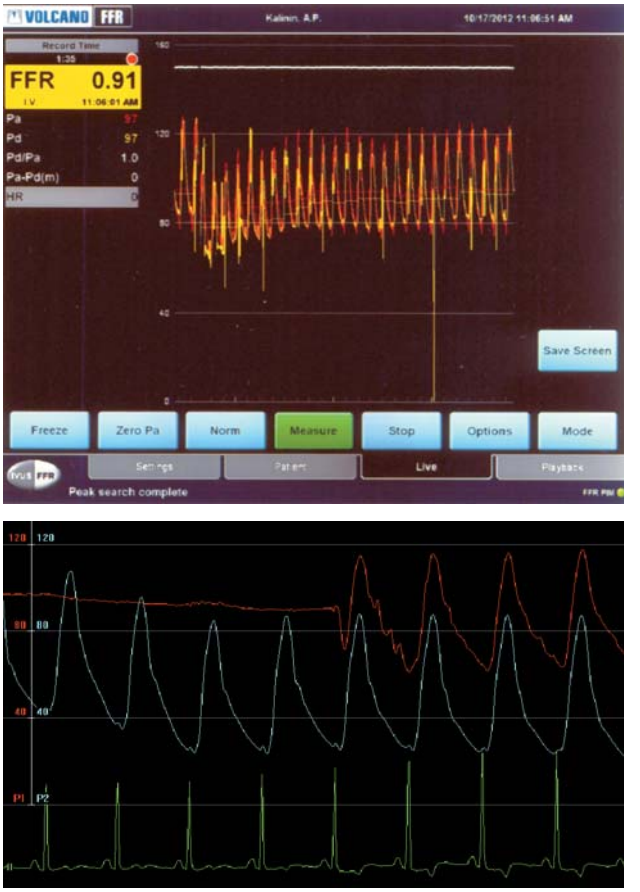

Figure 1. Measurement of FFR in the coronary artery after intracoronary administration of papaverine.

Intravascular ultrasound (IVUS) was performed on Volcano S5 apparatus (Volcano, USA), using Revolution 45 MHz mechanical transducer. In order to obtain high-quality image and to measure the length of a lesion, motorized device with constant movement speed of ultrasound transducer was used; longitudinal axis of the vessel was reconstructed. To prevent spasm, 200- 300 μg of nitroglycerin was administered intracoronary.

Fractional flow reserve (FFR) was measured by Radi Analizer (RADI, Sweden), and Volcano S5 (Volcano, USA) using specialized 0.014" manometric guidewire introduced through the mesh of implanted stent after intracoronary administration of papaverine at a dose of 20 mg for the left coronary artery (LCA) and 12 mg for the RCA (Figure 1).

Pressure probe was positioned 2 cm distally from the orifice to prevent Venturi effect associated with a drop of pressure in the region of tur-

Table 1. Results of quantitative coronary analysis and intravascular ultrasound, n = 152

Studied parameters	Study methods	
	Coronary angiography	IVUS
Extent of stenosis, mm	17.85 ± 5.16	29.36 ± 7.42
Reference diameter, mm	3.14 ± 0.28	4.12 ± 0.76
Minimal LD, mm	1.87 ± 0.19	1.12 ± 0.09
Minimal LA, mm^2	2.74 ± 0.42	1.86 ± 0.16
Minimal LND, %	65.51 ± 7.53	84.55 ± 2.67

Note: LD – luminal diameter; LA – luminal area; LND – luminal narrowing degree.

bulent blood flow. If FFR values were 0.75 or higher, stenosis of the side branch orifice was considered functionally insignificant (3, 5).

According to digital angiography data, reference segment diameter of the main branch was 3.14 ± 0.28 mm. The length of stenosis in the main branch was 17.85 ± 5.16 mm. Reference diameter of the side branch was 2.47 ± 0.29 mm. Extent of atherosclerotic lesion in the side branch orifice was 7.38 ± 3.37 mm. Comparative results of digital angiography and intravascular ultrasound of the target segment of main branches are provided in Table 1.

Therefore, comparative analysis of quantitative measurements using digital angiography and intravascular ultrasound revealed significant differences in all studied parameters. In particular, the extent of atherosclerotic lesion and vessel's reference diameter which are of key importance when choosing the stent were significantly higher ($p < 0.01$) according to the data of intravascular investigation.

A total of 170 patients were implanted 216 paclitaxel-eluting stents (Taxus, Boston Scientific). Mean stent diameter in the main branch was 3.65 ± 0.22 mm (3.5–4.0 mm). Mean stent length in the main branch was 31.33 ± 4.38 mm (24–38 mm).

There are no national guidelines on intravascular ultrasound criteria for optimal stent implantation. Therefore, in our study we were guided by suggestions of the Task Force of American College of Cardiology (2001) and by the results of clinical studies AVID, MUSIC, PRAVIO. Chosen criteria of non-optimal stent implantation were as follows: stent apposition towards the vessel wall; minimal luminal area in the stent < 70% of arterial reference segment area; stent expansion symmetry index less than 0.7. According to the data of control intravascular ultrasound, non-optimal stent implantation was revealed in 102 (60%) patients. The causes of non-optimal stent implantation were as follows: stent apposition towards the vessel wall – in 51.6% of cases; luminal area in the stent less than 70% of vessel area – in 25.8% of cases; stent expansion symmetry index less than 0.7 – in 22.6% of cases.

When analyzing immediate results of stent implantation obtained during intravascular ultrasound, the risk factors of non-optimal stent implantation were revealed (Figure 2). The most significant risk factors included the following: bifurcation proximal diameter exceeding the distal diameter by more than 0.5 mm (recalibration of the main branch of bifurcation) and the length of stenosis exceeding 20 mm. The less significant risk factor was eccentric location of stenosis (Figure 3).

Post-dilation in stents was performed only in 72 (42.4%) patients out of a total number of endovascular interventions.

According to the results of control measurements, the following should be noted: luminal area in stents was 31.2% more and residual stenosis was 59.8% less than corresponding values.

Therefore, the use of intravascular ultrasound made it possible to specify the diameter of the main branch of bifurcation, the length of the lesion and to determine the optimal sizes of stents during primary diagnostics; to reveal non-optimal stent implantation in 66.7% ($p < 0.05$) of cases during the control investigation among the patients with satisfactory angiographic stenting results.

At the stage of investigation, we did not manage to measure FFR of the side branch in six patients due to technical difficulties when introducing manometric guidewire through the mesh of implanted stent. Thus, we managed to measure fractional flow reserve of the side branch in 79 out of 85 patients, which constituted 46.7%. Fractional flow reserve value was 0.81 ± 0.08 in case of side branch orifice stenosis equal to 73.52 ± 9.78%.

Results of fractional flow reserve measurement in the coronary arteries are provided. Among 56 (70.9%) patients with 64.0–77.0%

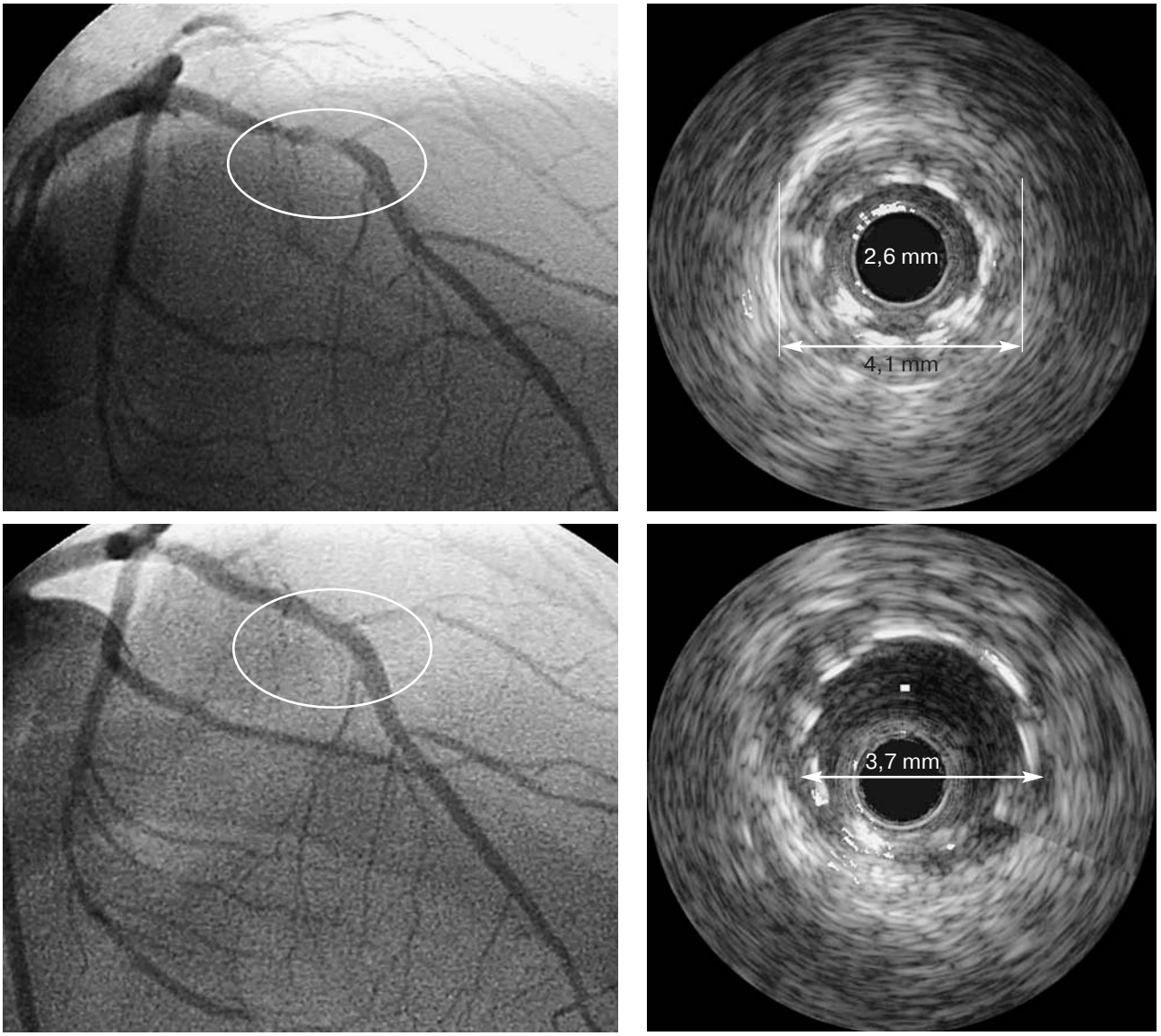

Figure 2. Balloon angioplasty of the LAD restenosis after non-optimal stenting

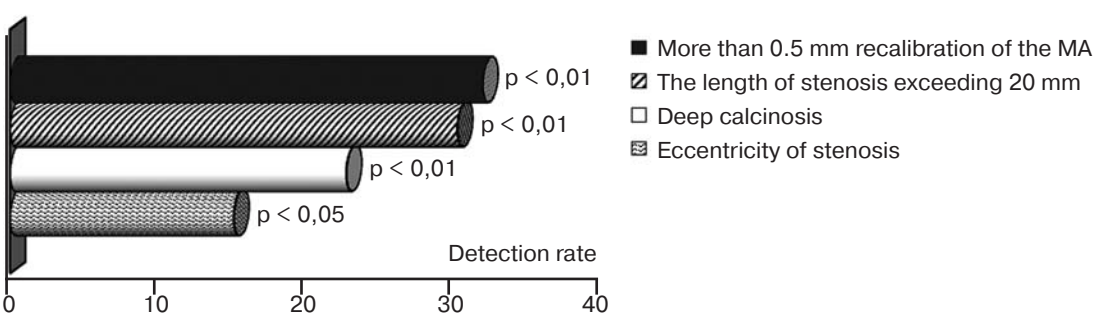

Figure 3. The risk factors of non-optimal stent implantation (intravascular ultrasound data)

narrowing of the side branch orifice, fractional flow reserve values were higher than the ischemic threshold (0.75). Out of 14 (17.7%) cases with 77.0–78.5% narrowing of the side branch orifice, fractional flow reserve values higher than 0.75 (71.4%) and lower than 0.75 (28.6%) were detected.

Angioplasty allowed us to achieve target value of fractional flow reserve; the ratio between diameter of the balloon catheter and arterial diameter was 0.83–0.85.

Thus, successful measurement of fractional flow reserve of the side branch after the stenting of the main branch of bifurcation was per-

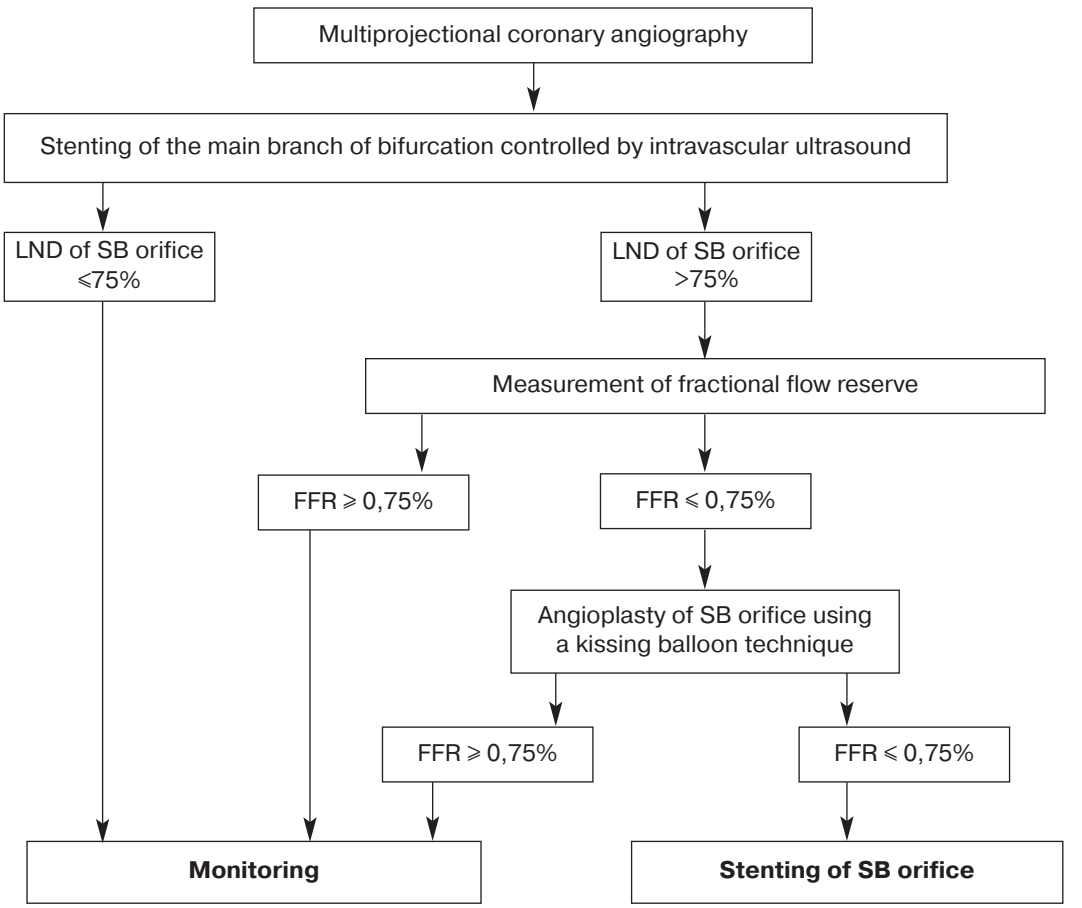

Figure 4. Algorithm of endovascular intervention during stenting of coronary artery bifurcation stenoses under the guidance of complex angiographic and intravascular investigations.

formed in the majority (93.3%) of patients. Fractional flow reserve value of less than 0.75 (indicative of stenosis functional significance) was detected only in 9 (5.3%) patients. Differentiated approach to the choice of endovascular intervention strategy based on fractional flow reserve measurement reduced the rate of angioplasty and stenting of the side branch orifice by 74.0%, respectively, and the incidence of side branch orifice dissection by 18.5%.

Total duration of procedure was 62.21 ± 7.24 minutes. Duration of fluoroscopy was 16.23 ± 2.25 minutes. The volume of used contrast medium was 280 ± 20 mL.

Despite the prophylactic measures, significant spasm of the target segment in the main branch developed in two patients (1.8%) manifesting in bradycardia, arterial hypotension accompanied by typical clinical presentation of angina pain. Intravascular investigation was successfully completed after stabilizing the patient's condition. In two (1.8%) cases, guiding of the ultrasound catheter through a tortuous segment of the main branch was complicated by linear intimal dissection and did not require additional stenting. Total percentage of complications associated with intravascular ultrasound was 3.6% which is comparable to the results (3.9%) of the largest study in 2207 patients from 28 USA sites (D. Hausmann D., 1995).

Placement of the guidewire for intravascular manometry in the side branch orifice was not accompanied by the increased incidence of intraoperative complications. No cases of intimal dissection, vessel perforation or guidewire fragmentation were observed. In 44 (25.9%) patients, intracoronary administration of papaverine was accompanied by the feeling of heat and pressure behind the sternum. In 22 (12.9%) cases, administration of papaverine was accompanied by transient changes on ECG which were as follows: T-wave inversion and ventricular extrasystoles. No life-threatening rhythm and conduction disturbances as well as the episodes of unstable hemodynamics were registered.

Positive immediate clinical result was achieved in all patients; it contributed to complete disappearance of angina and myocardial ischemia symptoms. Control treadmill test detected significant increase in physical load tolerance.

In 12 months, a decrease of physical load tolerance was observed in 6 (3.5%) patients as compared to the corresponding parameters during in-hospital period.

Based on the analysis of immediate and long-term treatment results, algorithm of endovascular intervention in CHD patients with coronary bifurcation stenoses was developed (Figure 4).

Thus, intravascular ultrasound and measurement of fractional flow reserve are safe methods of intravascular diagnostics which do not significantly increase radiation exposure, the volume of contrast medium, mortality rate and the incidence of intraoperative complications. Success rate of complex intravascular investigation during stenting of coronary artery bifurcation stenoses was 93.3%.

Measurement of fractional flow reserve during stenting of coronary artery bifurcation stenoses limited indications for endovascular intervention on the side branches: it decreased the rates of angioplasty and stenting of the side branch orifice by 48.8%.

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Successful Staged Stenting of the Vessels form Different Cardiovascular Terriotries in a Female Patient with Multifocal Atherosclerosis at High Risk for Coronary Artery Bypass Grafting (clinical case)

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To date, the problem of optimal tactics of management for multifocal atherosclerosis is still a matter of dispute. Concomitant atherosclerosis of the renal and brachiocephalic arteries increases the risk of perioperative complications during CABG. Our experience is suggestive of the ample opportunities and effectiveness of endovascular interventions in high-risk patients with multivessel atherosclerosis.

Key wodrs: *multifocal atherosclerosis, staged stenting, high-risk surgery, multiple stenting.*

Atherosclerosis is a systemic disease which often simultaneously affects different vascular basins. According to REACH International Registry data (2006), approximately 20% of patients with coronary heart disease (CHD), as well as with ischemic brain disease (IBD) or lower-extremity atherosclerotic arterial disease (LEAAD) have also symptoms of atherothrombosis in other vascular basins, and in approximately 2% of patients almost all vascular basins are involved in this process (1, 2, 3, 4). Moreover, the risk of atherosclerotic vascular lesions in general population increases with age. For example, the incidence of atherosclerotic renal artery lesions among people younger than 65 is 7–10% (K.J. Hansen et al., 2002), while in subjects older than 75 this pathology is observed in more than 40% of cases (C.J. Schwartz, T.A. White, 1964). In terms of prognosis as well as in terms of choosing an optimal treatment strategy, patients with multifocal atherosclerosis represent the most complex group of patients (5, 8).

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Manuscript received on March 27, 2013
Accepted for publication on April 28, 2013

The most widely used and optimal treatment of atherosclerotic lesions in vessels supplying different organs and tissues with blood is currently their surgical or endovascular revascularization. A number of multicenter studies proved that this also refers to the patients with multifocal atherosclerosis (6, 7). However, the problems regarding surgical strategy, scope of the surgery and the order of revascularization in this population of patients remain unsolved. Therefore, the problem of optimal treatment strategy in multifocal atherosclerosis currently remains topical. Especially this refers to the cases when we are facing a choice which myocardial revascularization method to select: endovascular or surgical. Naturally, when choosing a method of treatment we select the one which is less traumatic with similar efficiency and, equally important, the one which is less expensive and also is associated with a low risk of complications. In this context, endovascular method of treatment which meets the criteria listed above is intrinsically more preferable (9–11). Results of endovascular revascularization of different vascular basins in a female patient at high risk of surgical intervention (risk of complications and mortality according to STS database is 10.56%) are analyzed in this clinical case.

Female patient 67 years old was treated in the Moscow City Center of Interventional Cardiology diagnosed with: CHD. Functional class (FC) III exertional angina. Q-wave posterior diaphragmatic myocardial infarction (MI)

dated 2006. Arterial hypertension 90% stenosis of the left renal artery. Grade 1 chronic renal failure.

On admission to the in-patient department, the patient complained of angina attacks at rest and during exertion with short-term effect from nitroglycerin.

The patient noted the rises of blood pressure (BP) with maximum values up to 280/140 mmHg for a long time; she is adapted to 140/80 mmHg (while on hypotensive therapy). In 2006, she had *Q*-wave posterior diaphragmatic MI without preceding angina; she was treated conservatively in the in-patient department. MI had uncomplicated course. FC III angina attacks persisted in the future.

Analysis of patient's blood chemistry revealed increased level of cholesterol – 7.2 mmol/L, triglycerides – 2.7 mmol/L, urea – 10.8 mmol/L, creatinine – 130 μmol/L and potassium – 5.48.

According to ECG data, the following was observed: sinus bradycardia with heart rate of 45 beats per minute. Non-*Q*-wave scarry myocardial changes in the posterior wall of the left ventricle (LV).

According to EchoCG data, the following was observed: posterior wall hypokinesis. Ejection fraction (EF) was 56%. End-diastolic dimension (EDD) – 4.7 cm. End-systolic dimension (ESD) – 3.0 cm. Thickness of ventricular septum in diastole – 11 mm, 12 mm in the basal department. Thickness of the posterior wall in diastole – 10 mm. Moderate LV myocardial hypertrophy. Left atrium: 4.2 cm. Aorta was thickened, not dilated; sclerosis of aortic valve cusps was observed. On Doppler echocardiography, Grade 1 mitral regurgitation was detected.

Treadmill test was positive; typical angina pain accompanied by ECG changes (*ST*-segment depression in I, V3–V6 leads up to 1 mm) occurred on exertion (75 W/min). Physical load tolerance was low.

It was difficult to visualize renal arteries via ultrasound due to the postoperative scar on the anterior abdominal wall; nevertheless, it was managed to determine that the left kidney was decreased in size.

In order to study the state of coronary arteries and to choose further treatment strategy, the patient underwent diagnostic selective coronary angiography and left ventriculography (CAG and VG), abdominal aortography and selective angiography of the renal arteries due to severe course of arterial hypertension (AH) and low efficacy of hypotensive therapy (duration of imaging was 4.4 minutes; radiation

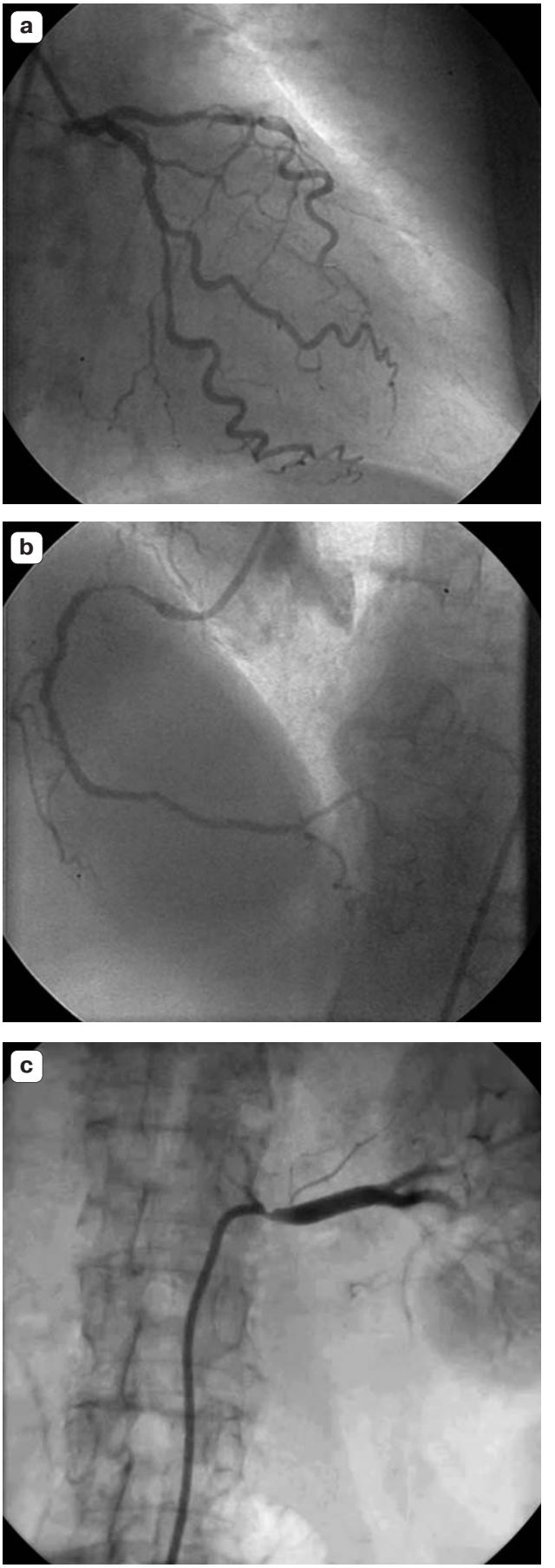

Figure 1. Diagnostic CAG of the LCA (a), RCA (b) and angiography of the left renal artery (c).

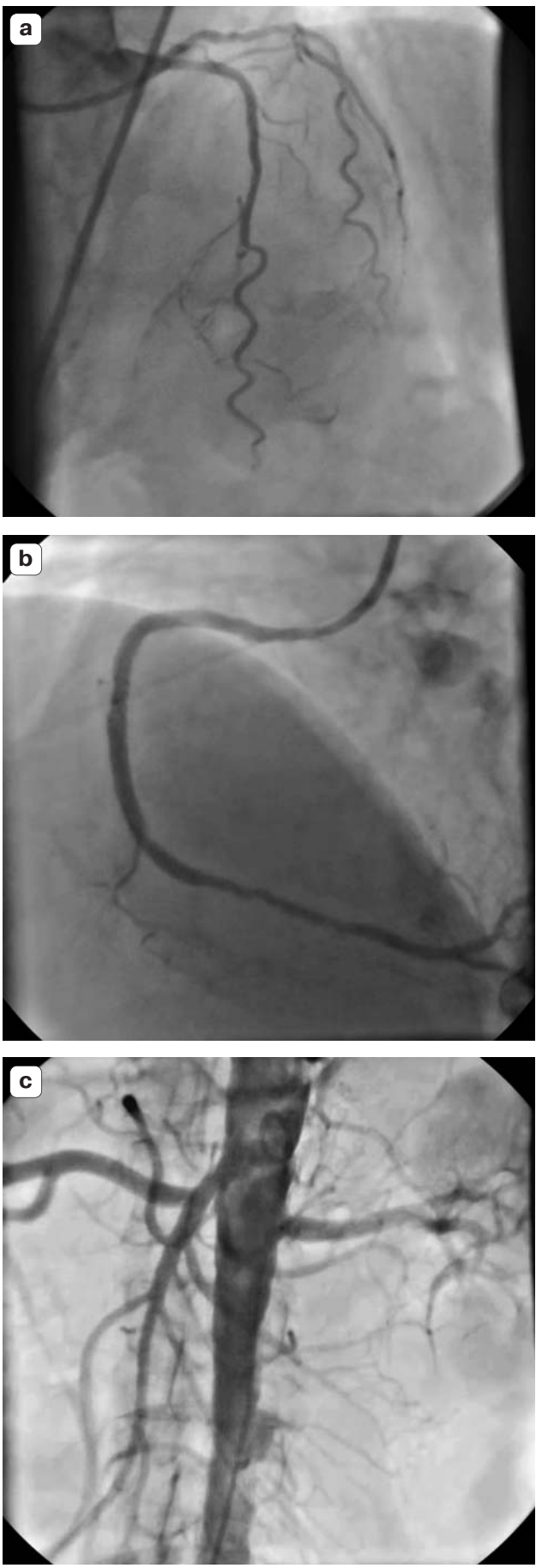

Figure 2. Immediate results of LAD (a), RCA (b) and left renal artery (c) stenting.

exposure was 1.6 mSv, contrast media consumption was 170 mL).

According to left ventriculography and selective coronary angiography, end-diastolic volume (EDV) was 127 mL. End-systolic volume (ESV) was 31 mL. LV EF was 78%. No asynergy zones were registered. The type of coronary circulation was right-dominant. The left main coronary artery was developed as usual, without changes. Left anterior descending artery (LAD) was calcified, with 75% stenosis in the proximal segment and 90% stenosis in the middle segment (Figure 1 a). Tandem stenosis up to 60% was revealed in the proximal part of the left circumflex coronary artery (LCX). Right coronary artery (RCA) had extended stenosis with maximum in the proximal segment (95%). Posterior descending artery (PDA) was occluded from the orifice; its distal segment was filled through the intersystem collaterals (Figure 1 b).

Angiography of the renal arteries: right renal artery (RRA) was stenosed in the orifice up to 40%. Left renal artery (LRA) was stenosed in the orifice approximately up to 90% (Figure 1 c).

Based on the obtained clinical angiographic and laboratory data, it was decided to conduct staged endovascular revascularization of different vascular basins impaired by stenotic atherosclerosis. As the first stage, we decided to conduct single-stage multiple stenting of the coronary arteries and the left renal artery orifice as an adequate alternative to surgical revascularization of these organs which is associated with higher risk of intra- and postoperative complications.

The patient underwent stenting of middle and proximal LAD segments (BX Sonic 2.75 × 28, BX Sonic 3 × 8 and BX Sonic 3 × 23 stents, respectively), as well as stenting of the proximal RCA segment at 2 levels (BX Sonic 3 × 28 and BX Sonic 3 × 23 stents, respectively), Figure 2 a, b. At the same time, direct stenting of the left renal artery via Eucatech AG 8 × 18 mm stent was performed, Figure 2 c. All endovascular procedures (EVP) were conducted with good angiographic result. Diseased arterial segment was fully covered by stents, vessel margins at the site of stent implantation were smooth and regular without stenotic changes (duration of imaging was 20.4 minutes, radiation exposure was 7.8 mSv, contrast media consumption was 350 mL).

Postoperative period was unremarkable, angina pain did not recur, BP dropped to 140/90 mmHg despite the fact that the daily dose of calcium antagonists was reduced. On Day 3 after the EVP, the patient underwent

dopplerography of the left renal artery; adequate intrarenal blood flow was observed, Vmax was 30 cm/sec, RI – 80. Blood chemistry also confirmed positive result of the EVP: the level of urea decreased from 10.8 to 8.8 mmol/L, the level of creatinine – from 130 to 103 μmol/L.

The patient was discharged under the supervision of specialists at her place of residence and recommended to regularly take Cardiomagnyl (at a dose of 75 mg/day), Plavix (75 mg/day), Concor (1.25 mg/day), Felodip (10 mg/day), Physiotens (8 mg/day), Liprimar (10 mg/day).

After conducted treatment and discharge from the in-patient department, physical load tolerance significantly increased, BP stabilized at the level of 130–150/80–90 mmHg.

11 months after conducted EVP, the patient was admitted to the Moscow City Center of Interventional Cardioangiology for control coronary angiography and angiography of the renal arteries and to work out further treatment strategy. On admission it was determined that 4 months after EVP angina attacks recurred, paroxysmal pressing pain occurred in the mesogastrium region along with bowel dysfunction.

According to blood chemistry data, hypercholesterolemia and triglyceridemia were detected: total cholesterol – 6.1 mmol/L, triglycerides – 2.1 mmol/L; the levels of urea (6.8 mmol/L), creatinine (93 μmol/L), potassium (4.2) were within the normal range.

ECG was without significant changes as compared to the previous one. Treadmill test was considered positive: typical angina pain accompanied by ECG changes (ST-segment depression in I, II, AVF, V5-V6 leads up to 1 mm) occurred on exertion (75 W/min). Physical load tolerance was low.

In-stent stenoses in the proximal and middle segments of the LAD and RCA were revealed on control CAG (Figure 3 a, b). On peripheral angiography of the superior mesenteric artery, 70% orifice stenosis was detected (Figure 3 c), Left renal artery (condition after the stenting) did not have signs of restenosis.

According to EchoCG and duplex scanning of brachiocephalic arteries, as compared to the results of 2007 investigation, no significant changes were observed. No signs of hemodynamically significant stenosis of the renal arteries were revealed. Hemodynamically significant stenosis (75–80%) in the orifice of the superior mesenteric artery was detected.

Taking into consideration data of coronary and mesenteric angiography, a decision was

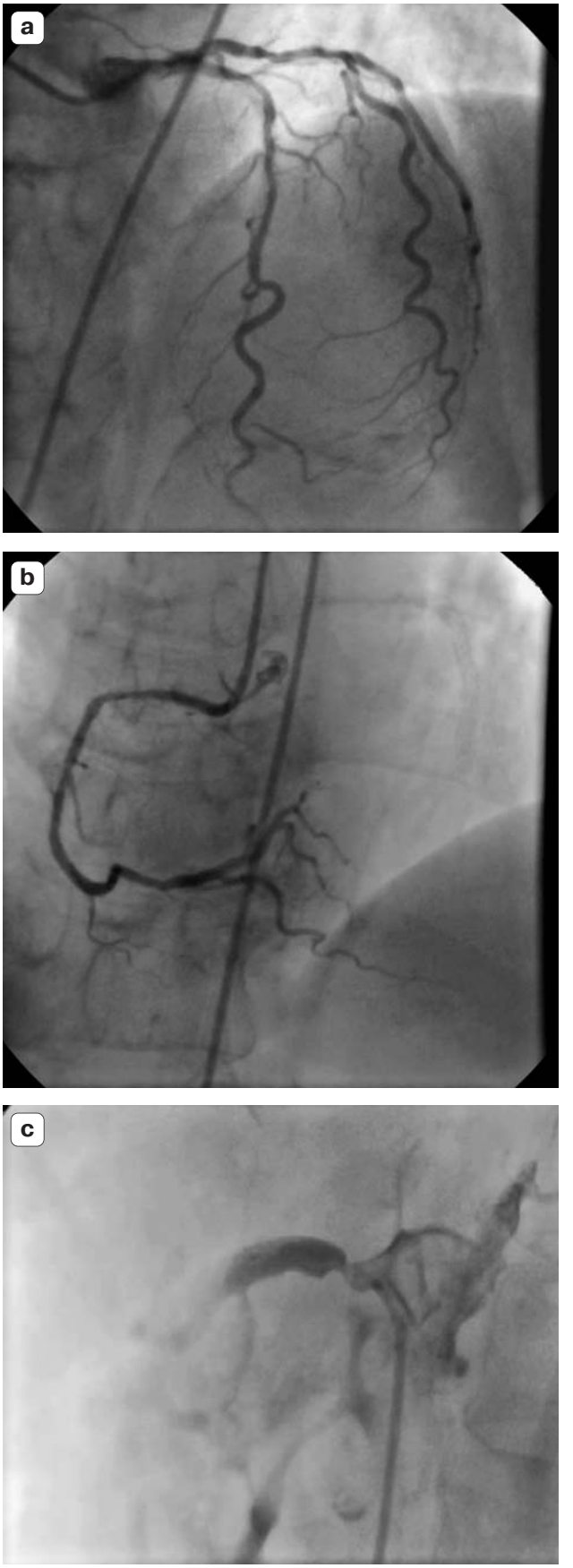

Figure 3. Diagnostic CAG of the LCA (a), RCA (b) and angiography of the superior mesenteric artery (c).

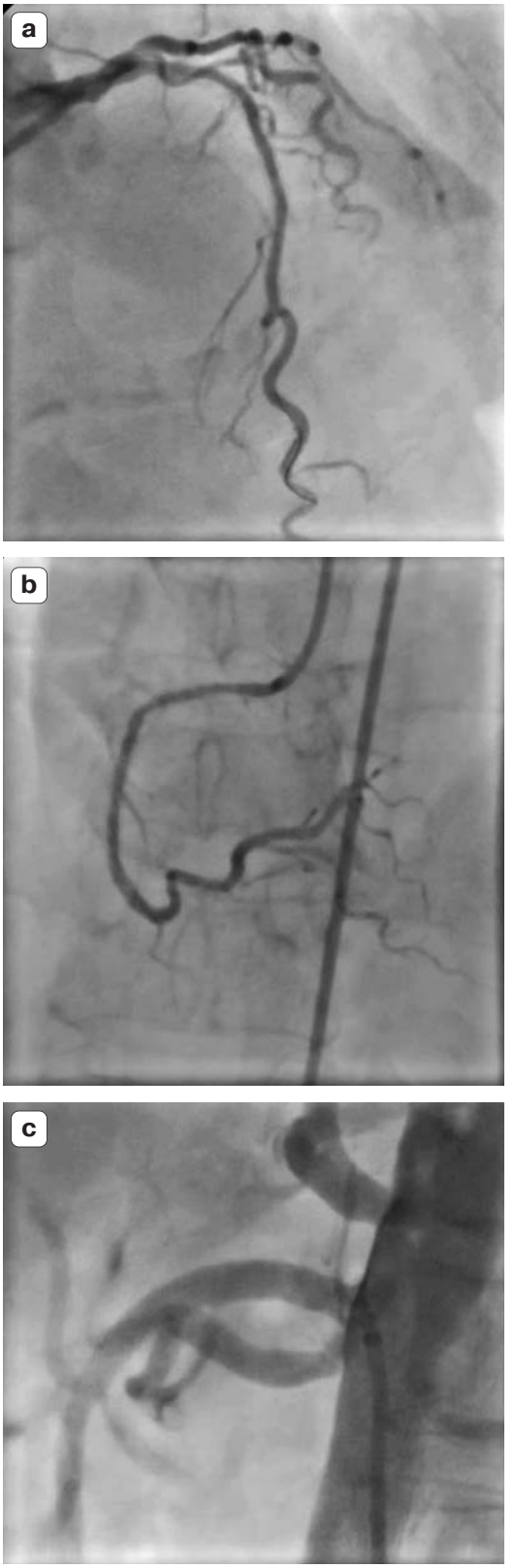

Figure 4. Immediate result of in-stent stenoses angioplasty on the LAD (a) and RCA (b), and stenting of the superior mesenteric artery (c).

made to conduct endovascular revascularization procedure in the specified basins. Single-stage angioplasty procedures of in-stent stenoses in the proximal and middle segments of the LAD and RCA (Figure 4 a, b), as well as balloon angioplasty and orifice stenting of the superior mesenteric artery via Euca STS flex 8 × 13 mm stent (Figure 4 c) were conducted with good immediate angiographic result. (duration of imaging was 9.6 minutes; radiation exposure was 3.7 mSv, contrast media consumption was 300 mL). Procedure and postoperative period were unremarkable.

The patient was discharged under the supervision of specialists at her place of residence, intake of the following drugs was recommended: Thrombo ASS – 100 mg/day, Plavix – 75 mg/day, Concor – 1.25 mg/day, Felodip – 5 mg/day, Physiotens – 8 mg/day. Due to hypercholesterolemia and triglyceridemia, the dose of Liprimar was increased up to 20 mg/day.

5.4 years after EVPs, in order to control the result of conducted treatment the patient was electively admitted to the clinics. On admission to the in-patient department she had no complaints. She noticed that physical load tolerance significantly increased. BP was at the level of 140/90 mmHg.

Blood chemistry analysis: total cholesterol – 4.9 mmol/L, triglycerides – 1.5 mmol/L; the levels of urea (6.8 mmol/L), creatinine (93 μmol/L), potassium (4.2) were within the normal range.

ECG, EchoCG data – without changes. Treadmill test was negative. Physical load tolerance was moderate.

According to the data of duplex vessel scanning, the state of brachiocephalic arteries was without significant changes. No signs of hemodynamically significant stenosis of the left renal and superior mesenteric arteries were revealed. >70% stenosis in the orifice of the right renal artery was detected.

On control coronary angiography of the LAD and RCA in the proximal and middle segments: status after stenting with no signs of restenosis (Figure 5 a, b). Peripheral angiography: superior mesenteric artery (status after stenting) with no signs of restenosis (Figure 5 c). Left renal artery (status after stenting) did not have signs of restenosis (Figure 5 d). Right renal artery was stenosed in the orifice up to 70% (Figure 5 f).

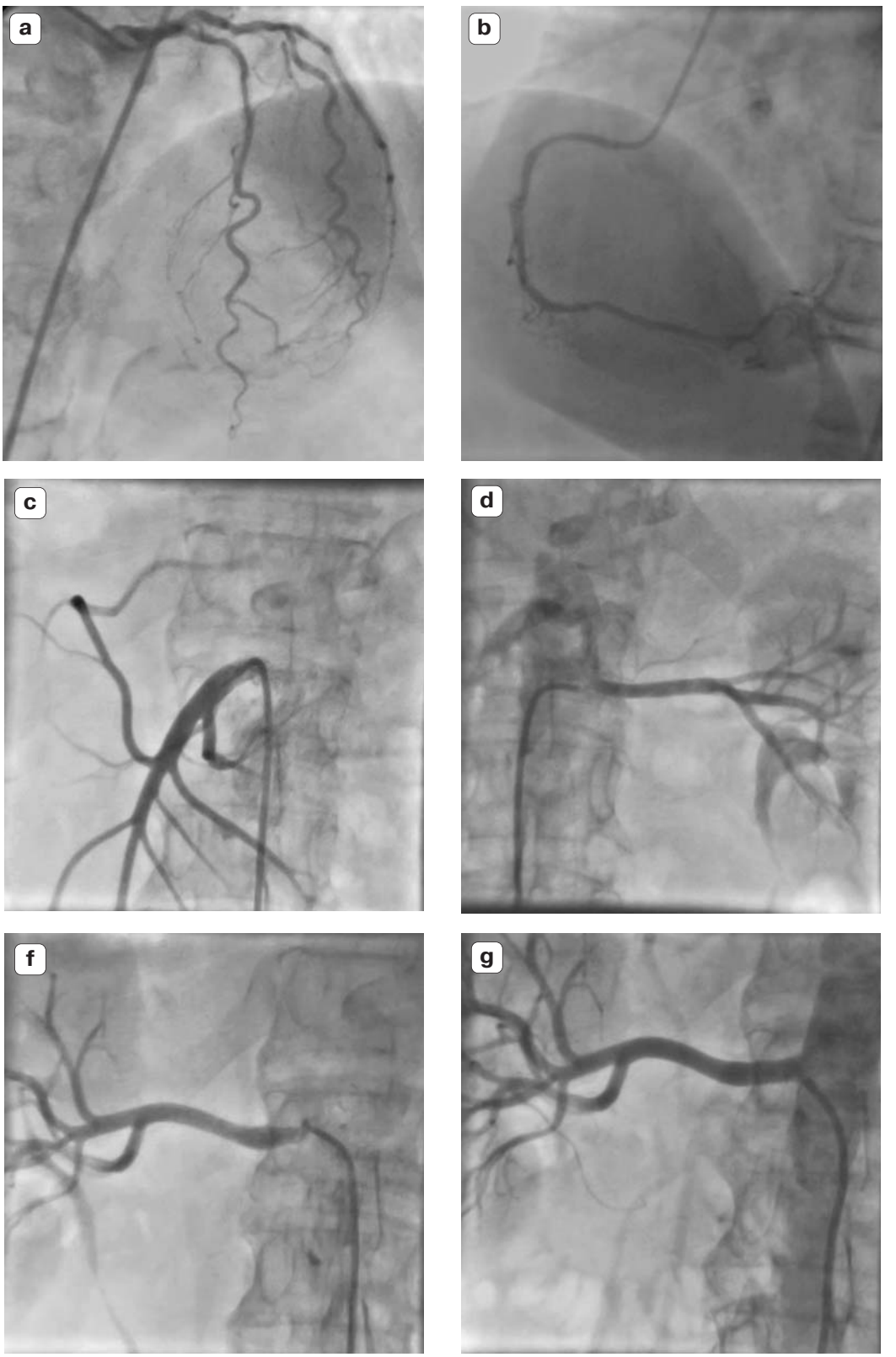

Figure 5. Diagnostic CAG of the LCA (a), RCA (b) and angiography of the superior mesenteric artery (c), left renal artery (d), right renal artery (f), final result of endovascular procedure (g).

Considering angiographic picture of progressive stenotic lesion in the right renal artery, the patient underwent balloon angioplasty and stenting of the right renal artery (Express Vascular 6 × 14 mm) with good immediate angiographic result (Figure 5 g) (duration of imaging was 6.4 minutes; radiation exposure was 1.9 mSv, contrast media consumption was 190 mL). Postoperative period was unremarkable, angina pain did not recur. Normalization of BP up to 140/90 mm Hg was clinically observed in a patient with intake of the daily dose of hypotensive agents. On day 3 after EVP according to Doppler sonography of the renal arteries, intrarenal blood flow on the right was adequate, no signs of hemodynamically significant stenosis were detected. Blood chemistry: urea – 7.8 mmol/L, creatinine – 84 μmol/L, potassium – 3.42. The patient was discharged in satisfactory condition.

Conclusion

In this clinical case we wanted to prove once more wide capabilities of endovascular revascularization for different organs. In this specific case, a female patient suffering from coronary heart disease, ischemic disease of kidneys and abdominal organs, i.e. with multifocal atherosclerosis, underwent endovascular revascularization procedures on cardiac, renal vessels and mesenteric artery. These procedures were conducted in stages with an interval of a few years; however, some procedures on different vascular basins were performed simultaneously. For example, multiple stenting of coronary arteries and renal artery stenting, as well as balloon angioplasty of in-stent stenoses in several coronary arteries and mesenteric artery stenting were conducted. Neither the patient nor medical staff exceeded acceptable radiation exposure limits; the doses of contrast agent allowed for single use were not exceeded as well. Such clinical cases once more confirm that endovascular methods of treatment have certain advantages over surgical methods such as no need in general anesthesia, artificial circulation, sternotomy and other surgical incisions; the fact that it is possible to conduct repeated endovascular interventions on the same object with no limitations which is rather problematic for surgical interventions is also very important. Also the fact that during endovascular interventions it is possible to simultaneously perform procedures on different basins as in this clinical case, which is rather difficult and sometimes impossible for surgical interventions, remains an advantage of endovascular treatment procedures over the surgical ones.

The second problem that should be pinpointed is in-stent stenosis when using bare-metal coronary stents. As we could see from the presented clinical case, in-stent stenosis was detected in 11 months via coronary angiography in two out of four bare-metal stents placed in the patient. However, considering the fact that angina recurred in the patient already in four months after placing the stents, it can be assumed that stent narrowing had occurred exactly by that time. It should be noted that optimal angiographic result was observed after placing them. It should also be noted that during the whole post-procedure period the patient was receiving combined therapy with plavix, thrombo ass and statins. This case once more confirms that it is advisable to place drug-eluting stents in problematic patients with severe coronary lesions and multifocal atherosclerosis.

And finally, successful revascularization of abdominal organs via mesenteric artery stenting accompanied by good clinical effect and disappearance of paroxysmal abdominal pain indicate that we should more actively and more often draw attention of physicians working at out-patient departments, ambulance and hospitals to the necessity of ultrasound examination of abdominal aorta branches in case of abdominal pain, especially in seniors, in order to detect acute stenotic lesions. This will allow endovascular or surgical revascularization procedures for ischemized abdominal organs to be performed in time.

Currently, the issue of optimal treatment strategy in patients with multifocal atherosclerosis remains controversial. Concomitant atherosclerosis of renal arteries and brachiocephalic arteries increase the risk of perioperative complications during coronary artery bypass grafting (5). The use of endovascular procedures (EVP) in these patients may decrease the scope of surgical intervention and thereby reduce the risk of complications. However, for combined endovascular and open surgeries, the risk of bleeding during antiplatelet therapy should be weighed in comparison with the risk of arterial thrombosis in case of therapy withdrawal in order to perform traditional surgical intervention.

Thus, this clinical case demonstrates the efficacy of endovascular intervention in patients with multifocal atherosclerosis at high

risk. High efficacy of used approaches and insignificant number of complications while implementing endovascular treatment methods are worth mentioning.

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A Clinical Case of Successful Closure of Post-Infarction Ventricular Septal Defect by Amplatzer Occluder on Day 4 from the Disease Onset

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A female patient with diabetes mellitus and acute transmural myocardial infarction complicated by cardiogenic shock caused by ventricular septum rupture, underwent successful closure of the defect with Amplatzer occluder on day 4 after the onset of the symptoms.

Key words: *Infarction, myocardial rupture, closure of postinfarction VSD.*

After the onset of an era with active use of reperfusion therapy in treatment of acute transmural infarction, the incidence of myocardial ventricular septal rupture, according to various sources, decreased by a factor of 5–6 and constituted 0.5% of all cases of acute transmural myocardial infarction (1–4) versus 1–3% if reperfusion treatment strategy was not used. Time of this complication development has also changed: from 3–5 days without any reperfusion therapy to 1 day in case of primary endovascular intervention or thrombolytic therapy (5, 6). In the majority of cases (70%), ventricular septal rupture occurs as a complication of anterior transmural myocardial infarction. Apical localization of the rupture is observed in 66% of cases, basal – in 34%.

It is known that the increased risk of myocardial rupture is associated with advanced age, female gender, diabetes mellitus, incident anterior transmural myocardial infarction, the absence of reperfusion within the first 3–6 hours from the onset of the disease, late drug-induced or mechanical reperfusion (3, 5).

Rupture of a free left ventricular wall in the vast majority of cases is a fatal complication of transmural infarction. In a majority of cases, ventricular septal rupture (VSR) is also a life-threatening complication for a patient, with in-hospital mortality rate exceeding 90%. Surgical or endovascular treatment aimed at closing ventricular septal defect (VSD) is the only chance to improve prognosis of the disease and to reduce the mortality rate to 35–45% (1, 2). At the modern stage of development of surgical and endovascular treatment methods, key issues in each particular case are as follows: to determine the optimal time for intervention, to choose the type of intervention, to determine an optimal pharmacologic and hemodynamic support at the stage of preparing the patient for correction of this complication and in the early post-operative period.

Case presentation

A female patient M., 59 years old, with a long history of insulin-dependent diabetes mellitus, arterial hypertension, overweight and no history of angina, in the morning of March 20, 2013 for the first time in her life experienced an intense burning pain behind the breastbone, sudden weakness, labored breathing, sweating. She did not seek qualified medical care and resorted to self-treatment including intake of non-steroidal analgesics, validol, valocordin. The above described pain maintained for a few hours with subsequent alleviation of the symptoms. On the following day, the patient noticed a progressive worsening of her condition which manifested in increased feeling of shortness of breath, at first – during minimal physical exertion (March 21, 2013), later - at rest (March 22, 2013), with development of gurgling breath (March 23, 2013), sharp weakness; meanwhile, chest pain did not bother her. In decompensated condition after a primary referral for medical care, the patient was brought by the Emergency Service team to the Cardiac Intensive Care Department of the City Clinical Hospital No 81 on March 23, 2013 at 12:30.

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Manuscript received on April 30, 2013
Accepted for publication on May 28, 2013

After a primary physical examination, according to the results of laboratory and instrumental investigations the patient was diagnosed with:

Coronary heart disease (CHD): acute anterior advanced *Q*-wave *ST*-segment elevation myocardial infarction dated March 20, 2013. Acute left ventricular aneurysm. Acute myocardial ventricular septal rupture. Sustained atrial fibrillation of unknown duration. Cardiogenic shock. Killip IV. Essential hypertension, stage III.

Community-acquired right-sided lower lobe pneumonia. Type 2 severe decompensated diabetes mellitus. Diabetic microangiopathy, retinopathy, polyneuropathy. Grade III obesity.

On serial ECGs in 12 standard thoracic and augmented leads, a frozen pattern typical for transmural anterior advanced myocardial infarction was registered.

It should be separately noted that an intensive systolic murmur in all standard positions with epicenter on the apex was heard on auscultation together with coarse respiratory murmurs. According to the echocardiography data, anteroapical acute left ventricular aneurysm, hyperkinesis of basal segments of the left ventricle (LV) and reduction of LV global contractility (ejection fraction (EF) = 42%) were detected. Detected defect (myocardial rupture) in the lower third of ventricular septum (8–10 mm in size) with massive left-to-right shunting and overload of the right departments (mean pulmonary arterial pressure (MPAP) – 86 mm Hg) was the cause of a coarse systolic murmur (Figure 1).

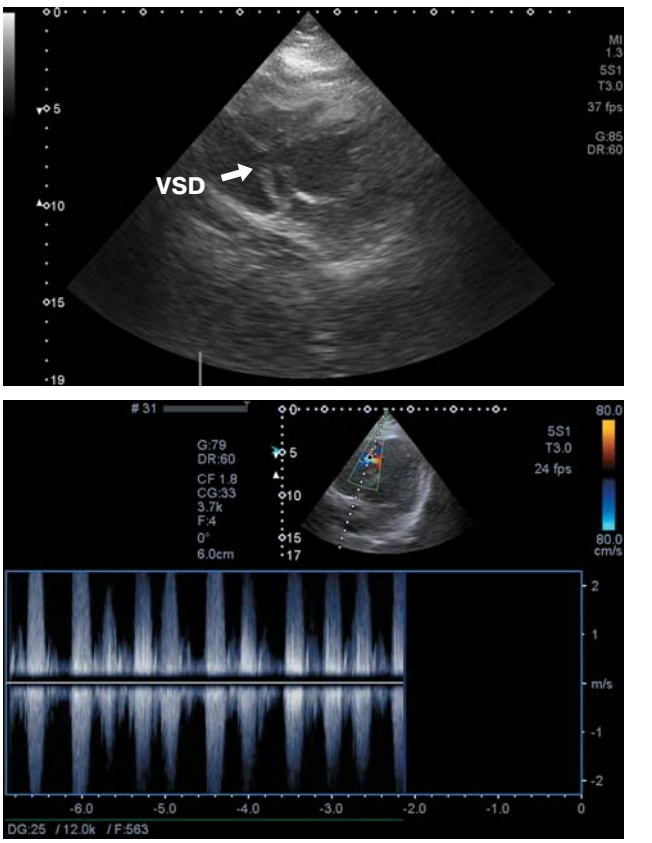

Figure 1. Post-infarction ventricular septal defect (rupture) with left-to-right shunting.

At the background of intensive therapy aimed at resolving clinical manifestations of circulatory failure, intra-aortic balloon counterpulsation (IABC) in 1 : 1 regimen was arranged which made it possible to achieve relative stabilization of main hemodynamic parameters and to resolve clinical manifestations of pulmonary edema. Against this background, on Day 2 (March 24, 2013) after admission to the Cardiac Intensive Care Department, coronarography (CG) and left ventriculography (VG) were performed to the patient; according to their data the following was detected: subacute magistral occlusion of the left anterior descending artery (LAD) in the proximal segment with no active collateral filling of a distal portion; moderate diffuse changes in the left circumflex coronary artery (LCX) and the right coronary artery (RCA); according to the data of the left VG in the left cranial projection the following was observed: ventricular septal defect with left-to-right shunting 10–12 mm in size. (Figure 2 a, b, c).

Considering the acute onset of ventricular septal rupture and incomplete formation and limitation of LV myocardial necrosis, an attempt to continue conservative treatment with IABC was made in order to achieve maximally safe time for the intervention (not less than 14 days). However, despite the conducted complex therapy under the control of invasive parameters of central hemodynamics and blood gases, the patient's condition began worsening. Due to progressive left and right ventricular failure refractory to conducted conservative therapy, on March 25, 2013 (on Day 3 from the admission and on Day 5 from the onset of acute myocardial infarction (AMI)), a decision was made to perform an attempt of endovascular closure of ventricular septal defect in the setting of combined endotracheal anesthesia and IABC. Taking into consideration location of the defect, transjugular right-sided approach using 10 Fr ASD delivery system was considered more preferable for formation of a transseptal arteriovenous loop. The guidewire was snared in the trunk of the pulmonary artery by a “spatial loop” (EN Snare, MERITMEDICAL) Figure 3 a, b. According to the current guidelines, VSD MI Amplatzer occluder was chosen with 30 mm waist diameter which was consistent with 2-fold exceeding of the defect size according to EchoCG data (Figure 3 a, b, c).

Directly after the closure of the defect, hemodynamic parameters stabilized which allowed us not to use cardiotonics immediately after the intervention. Moreover, a stable tendency towards arterial hypertension was observed in the immediate after-proce-

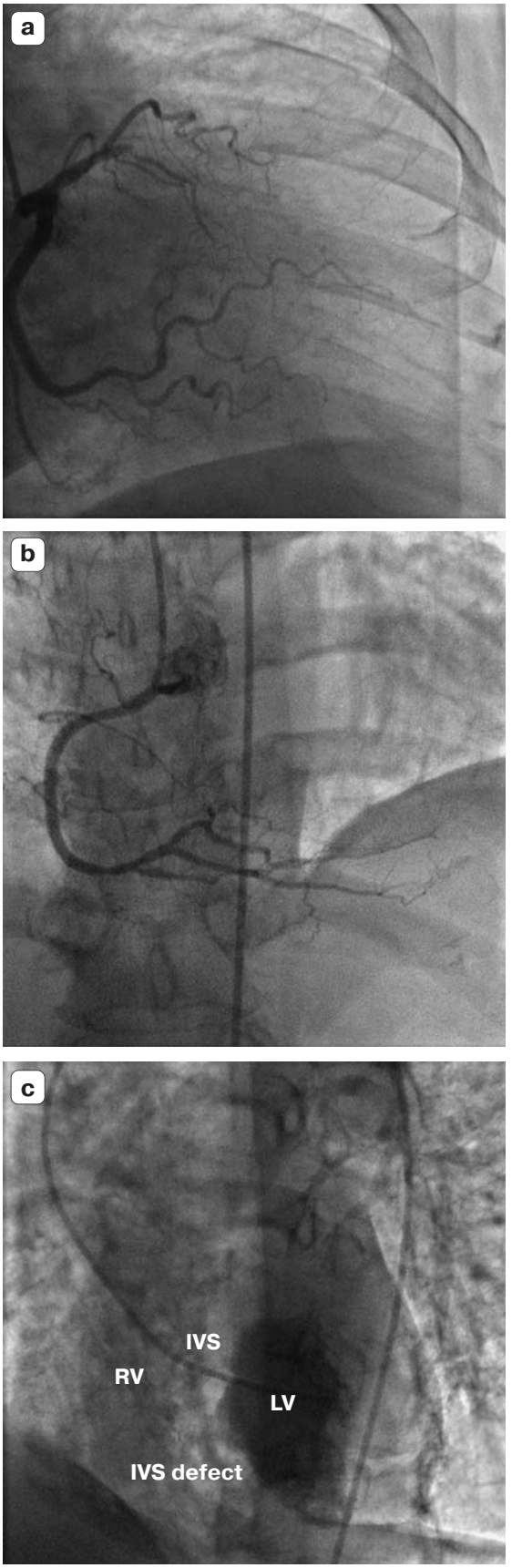

Figure 2. a – Subacute magistral occlusion of the LAD. b – Diffuse changes in the RCA. c – Left contrast ventriculography (LAO 40 Cr 20): IVS – interventricular septum; RV – right ventricle; LV – left ventricle.

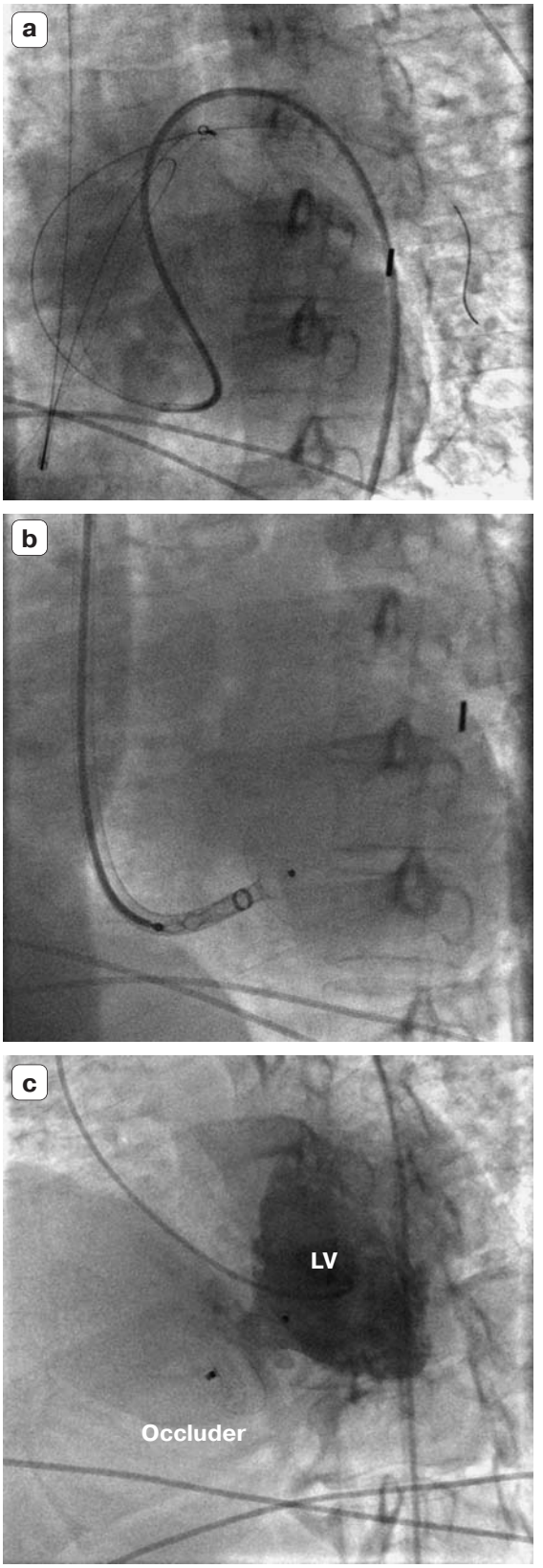

Figure 3. a – The stage of transseptal catheterization and snaring of a guidewire by a "spatial loop" (EN Snare, MERITMEDICAL) in the trunk of the pulmonary artery during IABC. b – The stage of expansion of a distal disc of Amplatzer occluder in the LV. c – Immediate angiographic result of Amplatzer occluder implantation procedure (left VG in the left oblique cranial projection).

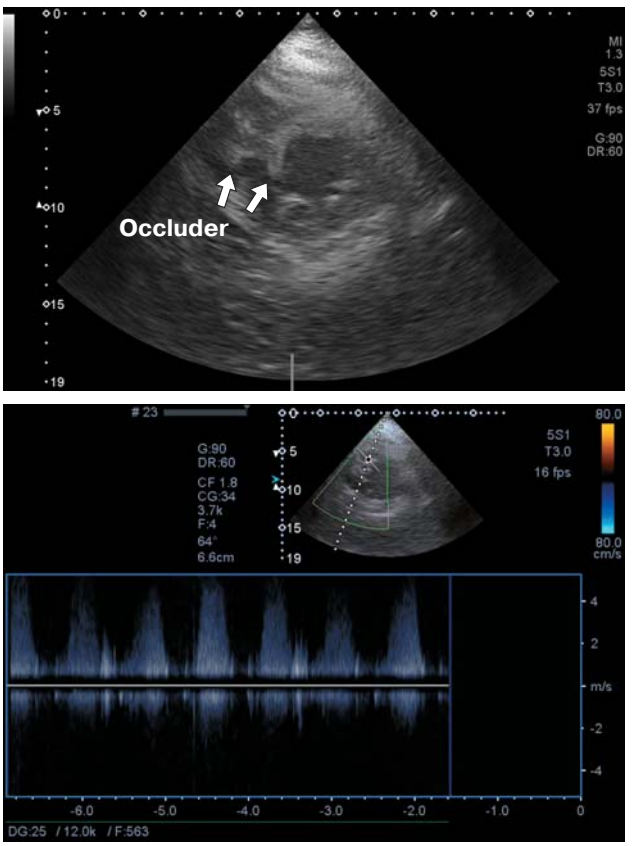

Figure 4. EchoCG directly after the procedure.

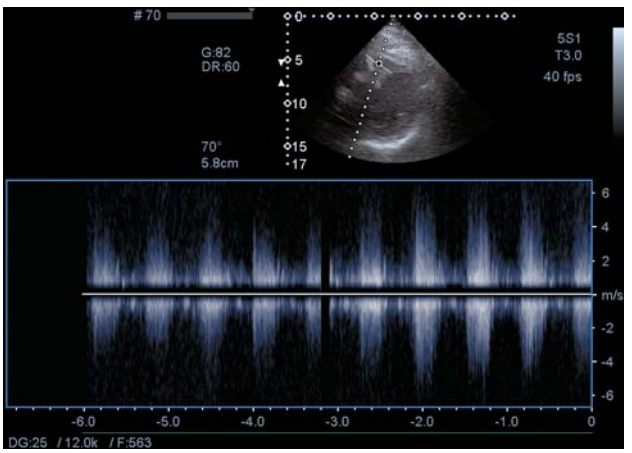

Figure 5. EchoCG 14 days after the procedure.

dural period. In order to decrease afterload (to reduce end-diastolic volume (EDV) of the LV), a decision was made to pharmacologically maintain moderate arterial hypotension (systolic arterial pressure not higher than 100 mm Hg) and to continue IABC for one more day.

According to EchoCG data, the following was observed over time after the intervention: correct occluder's position, decreased linear dimensions and volumes of the left and right ventricles, as well as disappearance of high-speed left-to-right shunting (Figure 4) with preservation of diffuse insignificant shunting due to so called porosity of occluder's body with subsequent progressive reduction of the latter and almost complete disappearance by Day 14 after the intervention (Figure 5). The patient was discharged from the in-patient department on Day 16 from the disease onset in satisfactory condition with moderate manifestations of circulatory failure at the background of conducted therapy.

Conclusion

The very fact of development of this threatening complication, its localization and time of development in our patient are consistent with current conceptions on this issue.

This clinical case, in our opinion, is characterized by a forced conduction of endovascular closure of ventricular septal defect rather early after the disease onset, when the processes of necrosis expansion and demarcation are not yet completed and the treatment outcome may be often worsened. We consider it right to refuse an attempt of late recanalization of the infarct-related left anterior descending artery as well as to continue conduction of intra-aortic balloon counterpulsation during moderate controlled hypotonia which helped us to provide maximally comfortable hemodynamic conditions in the early post-operative period.

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