

# International Journal of Interventional Cardioangiology

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# The First Russian Experience with Simultaneous Multiple Coronary Stenting and Transcatheter Aortic Valve Implantation

D.G. Iosseliani, A.G. Koledinsky, E.E. Kovaleva\*, I.V. Isaeva, A.N. Rogatova,  
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*The combination of surgical aortic valve replacement and aortocoronary bypass grafting is a "gold standard" for the treatment of patients with aortic stenosis and coronary heart disease (CHD). However in patients with high operative risk and in non-operable patients, transcatheter aortic valve replacement (TAVI) is performed instead of classic operation with increasing frequency. At present there is no clearly elaborated strategy for the timing and the choice of method for the treatment of CHD in patients referred for TAVI. Meanwhile, one of the eventual solutions is simultaneous, single-stage management of both pathologies.*

**Key words:** aortic stenosis, coronary heart disease, coronary arteries.

More than 50% of patients older than 70 years with severe atherosclerotic aortic stenosis are known to have coronary heart disease (CHD) caused by stenotic coronary atherosclerosis. Until recently, surgical aortic valve replacement combined with coronary artery bypass grafting was the "gold standard" treatment option for patients with combination of these heart diseases. However, it should be noted that many of these patients, especially geriatric subjects and persons with severe concomitant diseases have high risk of operative and postoperative complications as well as relative and absolute contraindications for a surgery using cardiopulmonary bypass (1, 2).

After endovascular transcatheter aortic valve implantation (TAVI) was introduced in clinical practice, combination of this method with percutaneous coronary intervention (PCI) may be considered as an alternative to surgical treatment in patients with high cardiosurgery risk (4). Therefore, there has appeared a need to radically revise indications and contraindications for both surgical and endovascular combined correction of atherosclerotic aortic valvular stenosis and coronary heart disease, i.e. to determine roles of every option for these pathologies treatment.

To date, the majority of investigators prefer endovascular options in geriatric and patients with severe somatic diseases with very high risks of serious complications in case of surgery with cardiopulmonary bypass. The same investigators consider the combined endovascular correction of aortic valve stenosis and stenotic coronary atherosclerosis to be more sparing and not less effective treatment option for these two diseases.

However, endovascular treatment options are also related to a wide range of unsolved problems. Sequence of treatment procedures is the most important issue. The majority of investigators consider that endovascular correction of coronary blood flow should be performed prior to aortic valve replacement. Their point of view is based on difficulty accessing coronary orifices due to prosthesis frame after valve replacement. Initial coronary artery stenting may also facilitate the second stage of treatment – transcatheter aortic valve implantation due to improved myocardial vascularization of the left ventricle. Therefore, restoration of affected coronary blood flow prior to transcatheter aortic valve implantation is more reasonable and requires no special consideration (3).

However, there is one more option to perform both endovascular procedures simultaneously, i.e. combine these treatments in one procedure. Unfortunately, only single articles on this issue are published, without any definitive conclusions.

Meanwhile, simultaneous endovascular and coronary and aortic correction is attractive for several reasons; the most important is less

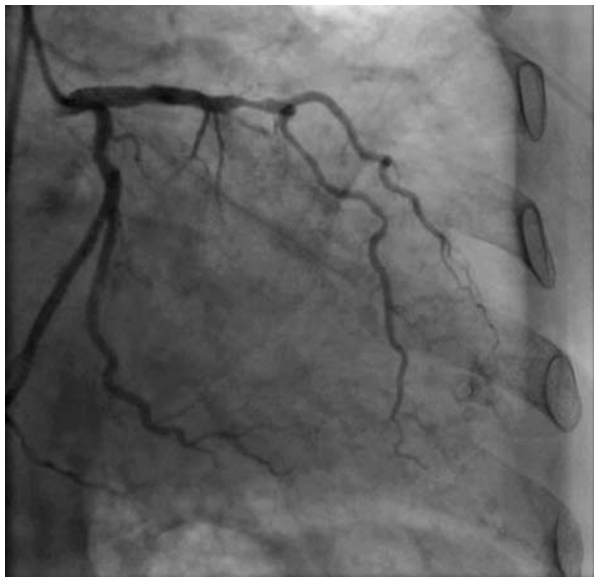
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**Fig. 1.** LCA. LAD stenosis and DB1 occlusion.



**Fig. 2.** LCA. LAD stenosis and DB1 occlusion.

emotional stress to a patient (one endovascular intervention is more preferable than two interventions), patient's in-hospital stay duration will be shortened, drug exposures will be reduced (quantity of mandatory medications used for any endovascular intervention will be decreased by 2 times) etc.

Therefore, we have been conducting the study to evaluate the results of simultaneous endovascular coronary stenting and aortic valve implantation since 2012. In accordance with the Protocol developed in our Center, coronary procedure is firstly performed, immediately followed by transcatheter aortic valve implantation.

Overall, in our Center transcatheter aortic valve implantations were performed in 16 patients using 17 prostheses (1 patient had 2 implanted prostheses). Out of them, 10 patients had combination of TAVI and PCI: 5 interventions were performed at different stages, and the remaining 5 interventions were done simultaneously. No deaths or dangerous clinical and interventional complications were seen. The second prosthesis (prosthesis-in-prosthesis) was used in one patient because the first prosthesis was not placed optimally (very high placement).

This report describes a clinical case of simultaneous multiple coronary stenting and transcatheter aortic valve implantation in a female patient with critical aortic stenosis of high risk and severe multiple coronary lesions.

Female patient, 77 y.o. was admitted to the Moscow City Center of Interventional Cardioangiography (MCCIC) with complaints of pressing chest pain and dyspnea on slight exertion.

There was no history of rheumatism and frequent sore throats. Since 2005 she has noted increased BP up to 170/100 mmHg; while treated with medications she was adapted to BP 140/80 mmHg. She has had chest burning and breathlessness during fast walking, i.e. angina attacks, since 2007. In the last year, she noted deterioration of dyspnea on exertion along with gradually decreased exercise tolerance. Severe aortic stenosis was firstly detected using EchoCG in March 2012 (peak pressure gradient between the left ventricle and aorta was 131 mmHg; mean gradient was 93 mmHg).

The patient was referred to MCCIC for additional examination and decision-making on further specialized medical care. Comprehensive clinical laboratory and instrumental exams were performed including selective coronarography: right type of the coronary blood flow was detected; the left main coronary artery was developed as usual, without changes; diffuse changes were throughout the LAD with the stenosis in the middle segment up to 80%; DB1 was occluded; moderate diffuse changes throughout the LCX and RCA without hemodynamically significant stenoses. Total lesion by SYNTAX scale was 6 (Fig. 1–5)

Cardiac cavities were not enlarged by EchoCG. The left atrium area is 19 cm<sup>2</sup>, the right atrium area is 16 cm<sup>2</sup>. The left ventricular contractility is satisfactory; the ejection fraction is 63%. End-diastolic diameter: 4.2 cm in the parasternal position; end-systolic diameter: 2.3 cm in the parasternal position; end-diastolic volume is 79 cm<sup>3</sup>; end-systolic volume is 18 cm<sup>3</sup>. Interventricular septum thickness in diastole is 16 mm; posterior wall thickness in diastole is 16 mm. There is significant symmetrical LV myocardial hypertrophy. The aorta is sclerotic; the ascen-

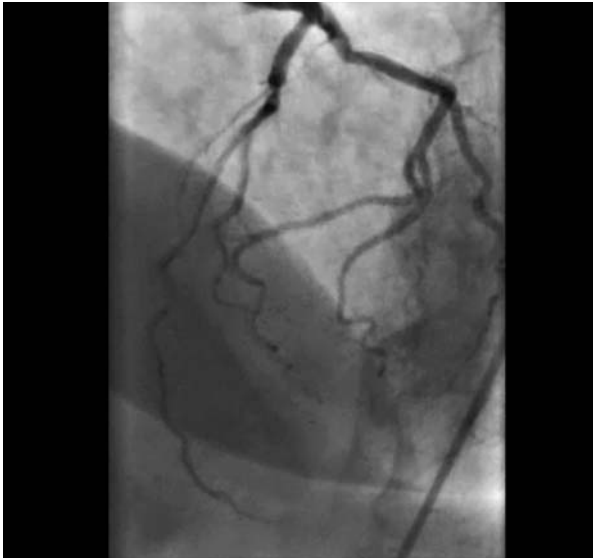


Fig. 3. LCA. LAD stenosis and DB1 occlusion.



Fig. 4. LCA. LAD and LCX stenosis.

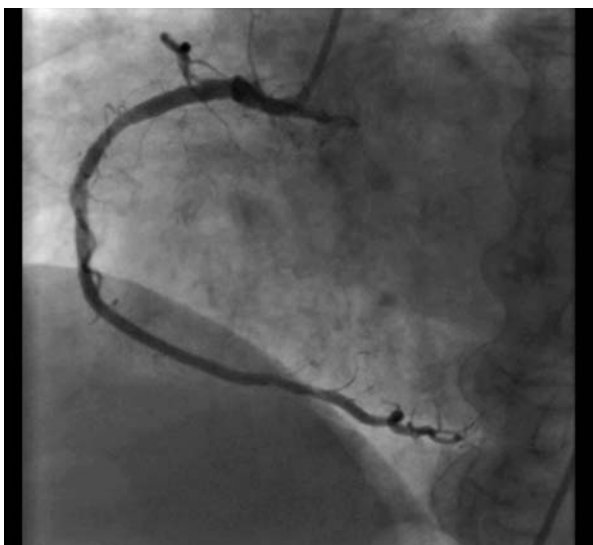


Fig. 5. RCA.

dant part is 2.83 cm, diameter at the level of sinotubular ridge is 1.95 cm, diameter at the level of Valsalva's sinuses is 2.7–3.0 cm, AV annulus diameter is = 1.7–1.9 cm, LV outflow tract diameter is 1.65 cm, Valsalva's sinus height is 1.6 cm. AV cusps are calcified. Doppler echocardiography: Degree 0–1 regurgitation into the LV, **AV systolic flow speed = 5.7 m/sec, peak systolic gradient is 131 mmHg, mean systolic gradient is 93 mmHg, estimated AV orifice area is 0.4 cm<sup>2</sup>**. The aortic valve is significantly stenosed. Mitral valve: cusps are indurated with calcium inclusions, the cusps move in different directions. Doppler echocardiography: mean diastolic gradient is 2.68 mmHg, Degree 2 regurgitation into the LA. Tricuspid valve: the cusps moved in different directions. Doppler echocardiography: degree 1 regurgitation into the RA, **mean pulmonary artery pressure (MPAP) = 46 mmHg**. There is moderate pulmonary hypertension. (Fig. 6–8)

Electrocardiography: sinus rhythm, HR = 60 bpm. Left anterior fascicular block. There were the signs of left ventricular myocardial hypertrophy. (Fig. 9)

At 24-hour ECG monitoring, sinus rhythm was registered: minimal HR 57 bpm; maximal HR 104 bpm; mean HR 68 bpm. Left anterior fascicular block.

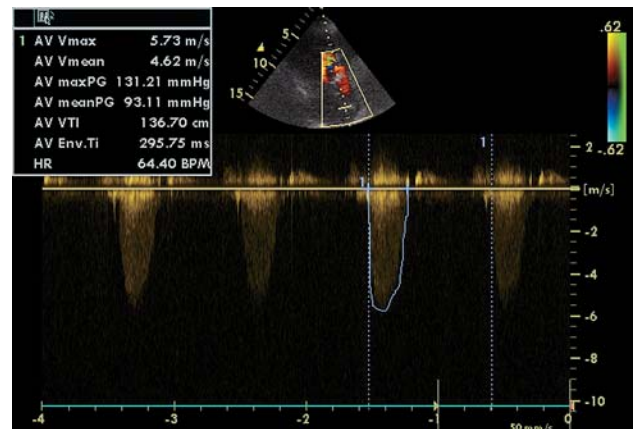


Fig. 6. Pre-interventional EchoCG. AV pressure gradient measurement.

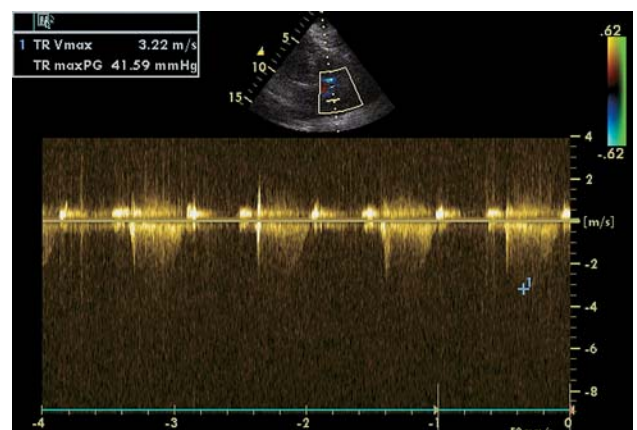
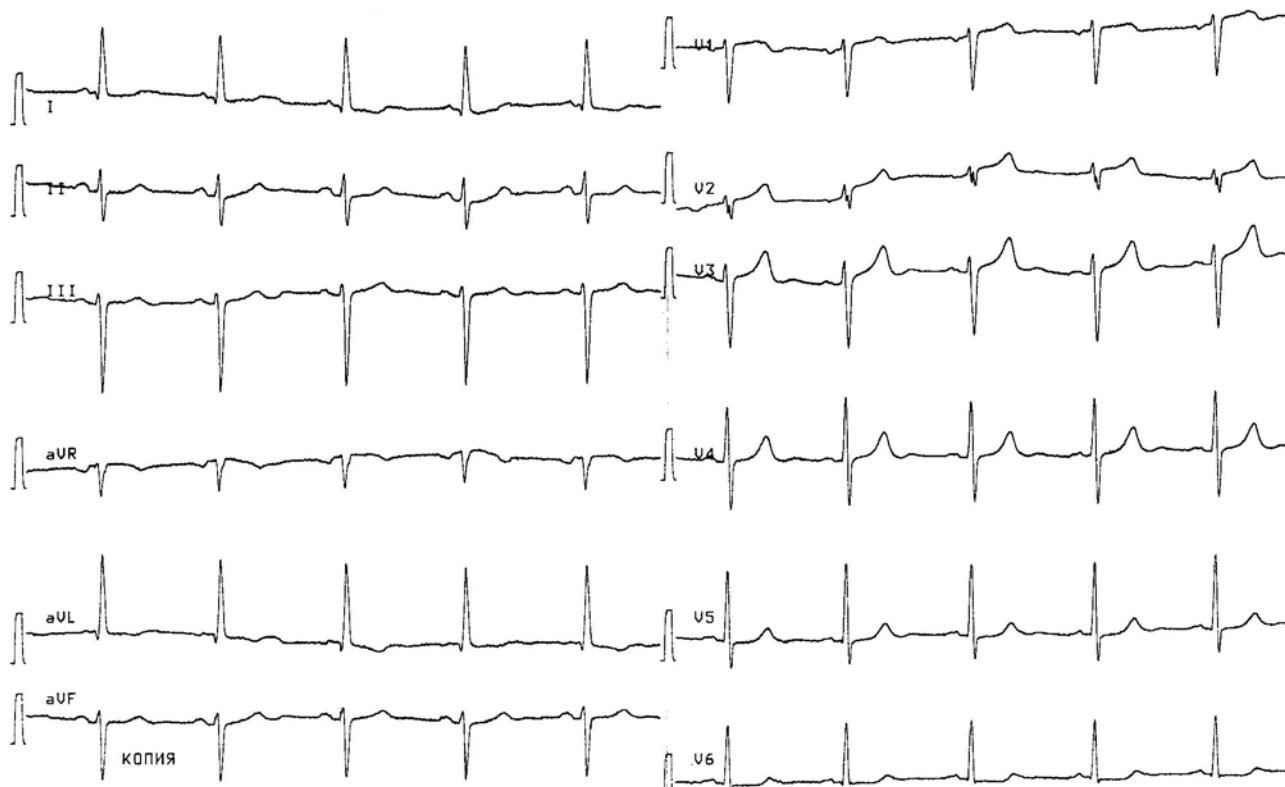


Fig. 7. Pre-interventional EchoCG. Pulmonary artery systolic pressure.



**Fig. 8.** Pre-interventional EchoCG. Significant myocardial hypertrophy of the left ventricle.



**Fig. 9.** Pre-interventional ECG.

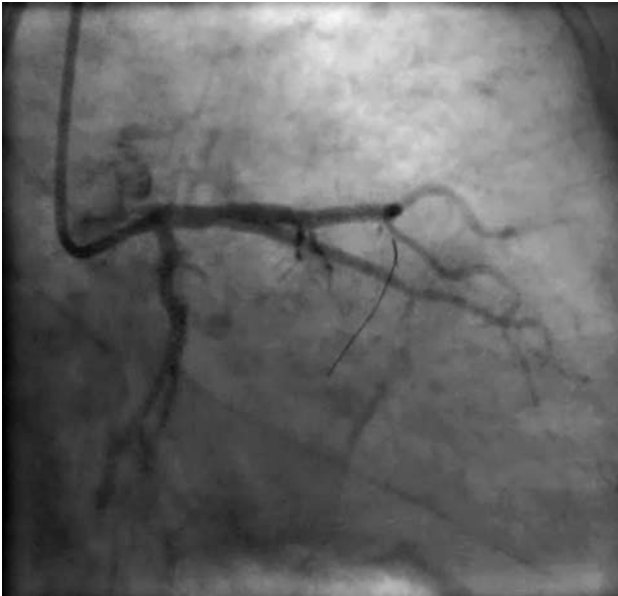
There were single premature ventricular and supraventricular contractions. Myocardial ischemia accompanied with ST shift from the isoelectric line up to 3 mm on exertion was detected.

No laboratory abnormalities were detected.

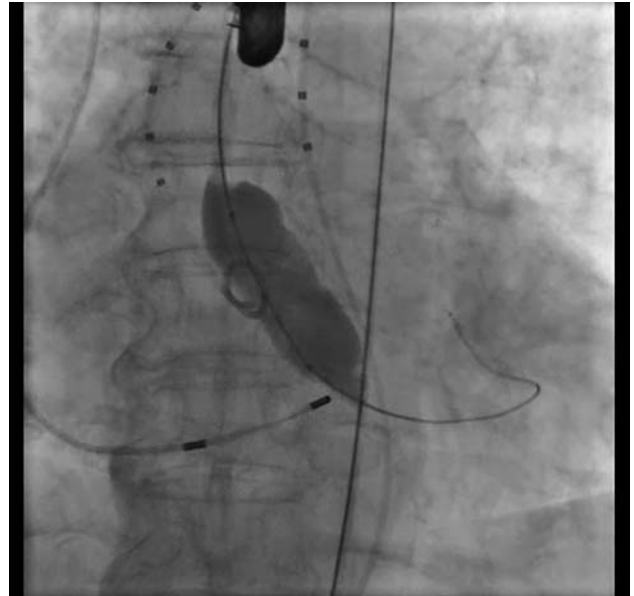
The decision on simultaneous coronary stenting and transcatheter aortic valve implantation using CoreValve prosthesis was made. Firstly, the mechanical recanalization, PCTA and stenting of the DB1 (Xience V  $2.25 \times 12$  mm and Xience Prime  $2.25 \times 23$  mm) and direct stenting of the middle part of the LAD were performed (Xience Prime  $3.5 \times 12$  mm.) (Fig. 10). Secondly, after myocardial revascularization, transcatheter aortic valve implantation was per-

formed using CoreValve system 26 mm. Under general anesthesia, right common femoral artery was isolated, punctured and introducer sheath 18 Fr was placed in it. Then, left common femoral artery was punctured and introducer sheath 6 Fr was placed in it. Two pigtail catheters 5 Fr were passed through the introducer sheaths and placed into the aorta and LV. Mean pressure gradient between the left ventricle and aorta was 90 mmHg. An electrode for temporary pacing was placed into the RV through the right internal jugular vein puncture. Balloon catheter was inserted over the wire in the area of aortic valve, and aortic valve was dilated when the heart was paced at 180 ppm. Then, CoreValve system 26 mm was

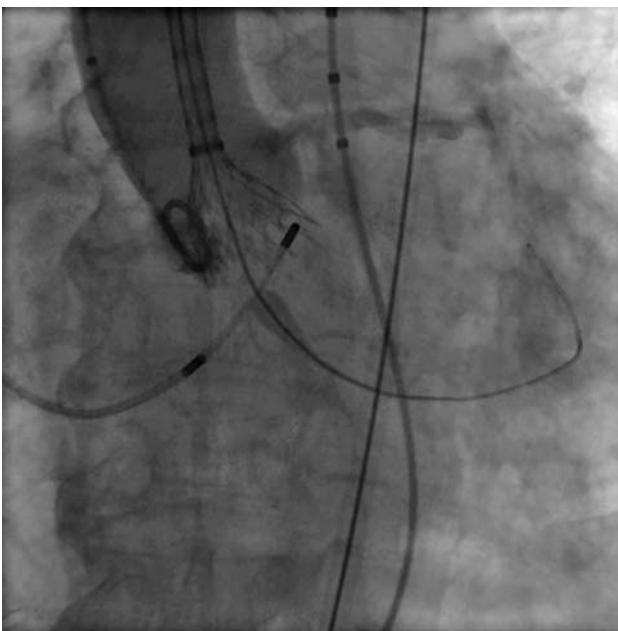




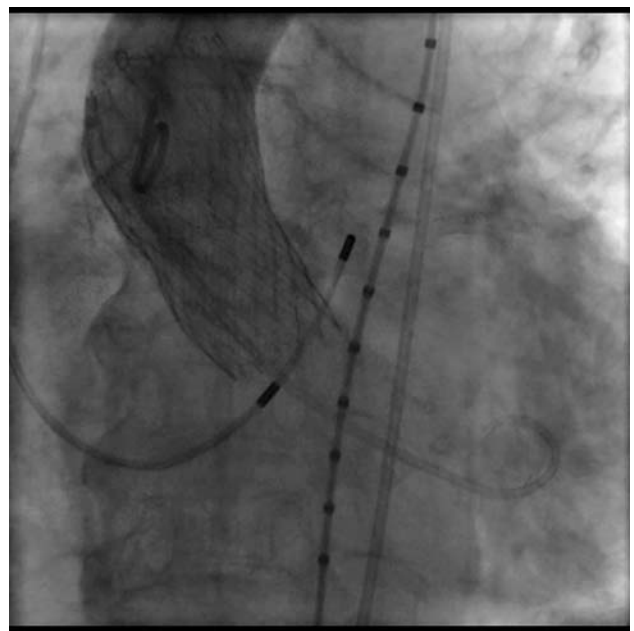
**Fig. 10.** Mechanical recanalization, PCTA and stenting of the DB1 (Xience V 2.25 × 12 mm and Xience Prime 2.25 × 23 mm) and direct stenting of middle part of the LAD (Xience Prime 3.5 × 12 mm).



**Fig. 11.** Balloon aortic valvuloplasty.



**Fig. 12.** Aortic valve prosthesis positioning and expansion.

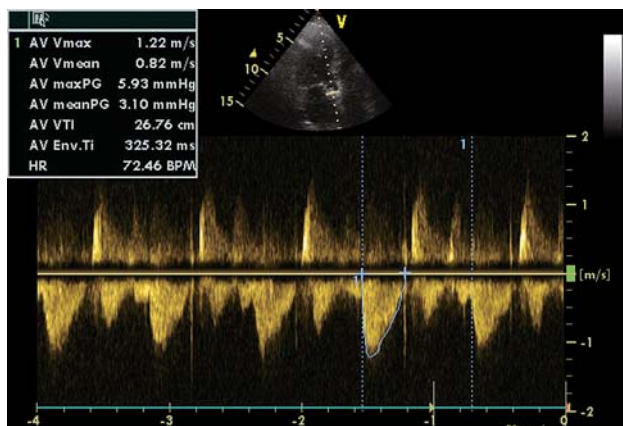


**Fig. 13.** CoreValve Systems 26 mm aortic valve prosthesis implantation.

inserted on the delivery device in the area of aortic valve, and it was implanted in accordance with generally accepted method (Fig. 11–13). No aortic regurgitation was observed during the control aortography. At control examination, mean gradient was 9 mmHg. The intraoperative transesophageal echocardiogram (TEEG) showed aortic prosthesis, aortic regurgitation was minimal. The prosthesis function was satisfactory. Peak gradient was 11 mmHg. The pericardial cavity contained no liquid (Fig. 14). Total duration of all procedures was 133 min; fluo-

roscopy time was 40.3 min, contrast media consumption was 350 ml.

*Clinical diagnosis:* Acquired valvular heart disease. Severe aortic stenosis. CHD. FC 2 effort angina. Left anterior fascicular block. Essential hypertension, stage II. Circulatory insufficiency, class 1 NYHA FC 2. State after mechanical recanalization, PCTA and stenting of DB1 (Xience V 2.25 × 12 mm and Xience Prime 2.25 × 23 mm), direct stenting of the middle part of the LAD (Xience Prime 3.5 × 12 mm) dated December 17, 2012. State after transcatheter



**Fig. 14.** Post-interventional EchoCG (before discharge). AV mean pressure gradient.

aortic valve implantation using CoreValve Systems 26 mm dated December 17, 2012. Dyslipidemia 2B.

*Concomitant diagnosis:* Type 2 moderate and compensated diabetes mellitus.

Therefore, this clinical case demonstrates that simultaneous transcatheter aortic valve

implantation and multiple coronary stenting in the female patient with critical aortic stenosis of high risk and coronary heart disease was possible and safe.

## References

1. Dewey T.M., Brown D.L., Herbert M.A. et al. Effect of concomitant coronary artery disease on procedural and late outcomes of transcatheter aortic valve implantation. *Ann Thorac. Surg.*, 2010, 89 (3), 758–767.
2. Dimarakis I., Rehman S.M., Grant S.W. et al. Conventional aortic valve replacement for high-risk aortic stenosis patient not suitable for transcatheter aortic valve implantation: feasibility and outcomes. *Eur. J. Cardiothorac. Surg.*, 2011, 40 (30), 743–748.
3. Gautier M., Pepin M., Himbert D. et al. Impact of coronary artery disease on indication for transcatheter aortic valve implantation and on procedural outcomes. *Eurointervention*, 2011, 7 (5), 549–555.
4. Conradi L., Seiffert M., Franzen O. et al. First experience with transcatheter aortic valve implantation and concomitant percutaneous coronary intervention. *Clin. Res. Cardiol.*, 2011, 100 (40), 311–316.



# Manual Vacuum Thrombextraction in Combination with Endovascular Angioplasty of Infarct-Related Artery in STEMI Patients: Immediate Clinical and Angiographic Results

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*It is known that the presence of visible parietal thrombus in the infarct-related artery compromises short-term, as well as long-term outcomes of endovascular treatment of patients with acute myocardial infarction (AMI). As a rule, it happens due to intra-procedural distal embolization of the coronary bed. According to several authors, manual vacuum thrombextraction (MVT) is one of the most effective methods for the prevention of this complication. We present the experience of Moscow City Center of Interventional Cardioangiologiy with MVT in 75 AMI patients.*  
**Key words:** acute myocardial infarction, thrombextraction, endovascular procedures.

Diagnostics and treatment of acute myocardial infarction have dramatically changed over the past 30 years, thus significantly reducing in-hospital mortality from 20–25% to 3–7%. Firstly, this became possible due to wide clinical implementation of effective medications, cardiac supportive methods, and, most importantly, urgent coronary angioplasty (endovascular procedure, EVP). This procedure helps restore blood flow in infarct-related artery (IRA), thus considerably improving hospital prognosis for AMI patients: to decrease serious cardiac morbidity and mortality rates (1, 2, 3). However, in some cases when EVP is used, despite optimal angiographic results (opacification along the whole IRA length, no residual stenosis or signs of serious vessel dissection), patient's clinical state during the procedure worsens, i.e. status anginosus relapses, myocardial ischemia occurs and left ventricle functional capability reduces (4). Therefore, there is some inconsistency between angiographic and clinical data. In opinion of majority of investigators, one of the most important reasons for this phenomenon may be deterioration of myocardial perfusion at the microcirculatory level due to coronary distal embolization with fragments of thrombus during EVP (5). Therefore, the inves-

tigators have started to search for optimal pharmacological or mechanical options to protect coronary vessels from distal embolization during EVP (6, 7, 8). One of these options for preventing both macro- and microembolization is manual vacuum thrombextraction (MVT) making it possible to remove thrombi from the IRA, completely or partially. The first successful vacuum extraction of thrombus from the proximal part of the right coronary artery using the guide was reported by Lablanché who performed this procedure in 1989 (9). As a result of further improvement of MVT devices and accumulation of clinical experience, this option became important for AMI treatment. This was demonstrated in several multicenter, randomized trials (DEAR-MI, 2007; TAPAS, 2008; EXPIRA, 2009) (10–12). These studies based on data analysis from many AMI patients demonstrated superiority of manual vacuum thrombextraction over routine EVPs in the IRA, both with immediate and long-term angiographic and clinical results. However, to date, there are no clear indications for the above option. Therefore, further accumulation of experience and thorough comparative analysis of this option compared with different devices intended for MVT are required. It prompted us to conduct a study based on MVT results in AMI patients treated at the Moscow City Center of Interventional Cardioangiologiy from January 2008 to September 2012. During this time period, 152 manual vacuum thrombextractions from the IRAs were performed in patients within the first hours of AMI.

The primary objective of this study is to compare the efficacy and safety of MVT in combina-

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**Table 1.** Baseline clinical, historical and laboratory data of studied patients

Characteristics	Group 1 (n = 75)	Group 2 (n = 74)	P
Age (years)	55.4 ± 8.2	51.3 ± 10.6	NS
Sex (male)	85.7 ± 9.3	82.4 ± 7.4	NS
AH, %	62	54.8	NS
Hypercholesterolemia, %	58	55.9	NS
Diabetes mellitus, %	8	6.5	NS
AMI (history), %	6	5.2	NS
EVP (history), %	2	0.0	NS
CABG (history), %	2	0.0	NS
CVA (history), %	0.0	2.6	NS
Smoking, %	76	82.4	NS
CAD duration (months)	7.5 ± 4.2	5.8 ± 5.1	NS
AMI localization			
Anterior, %	50.6	56.1	NS
Posterior, %	49.4	43.9	NS

tion with urgent EVP in AMI patients. In addition to clinical and laboratory data, the results were analyzed using antegrade blood flow in the IRA by TIMI (6, 7); MBG (13); ST dynamics (14) in two adjacent ECG leads; blood levels of cardiospecific enzyme CPK-MB over time.

### Characteristics of patients and study methods

The study was retrospective and included 149 STEMI patients. They were divided into 2 groups: Gr.1 (n = 75) included patients after MBTE combined with EVP; Gr.2 (n = 74) consisted of patients after EVP only.

Study inclusion criteria were as follows: clinical presentation of AMI; EVP performed not later than 6 hours after the onset of angina attack; ST elevation >0.1 mV in two adjacent ECG leads; angiographic signs of thrombus in the IRA (TBG ≥ 2) (15). Exclusion criteria were as follows: left ventricle ejection fraction <25%; acute myocardial infarction of the right ventricle; cardiogenic shock; main LCA lesions; pre-hospital systemic thrombolysis; acute or chronic renal or hepatic failure; serious hematopoietic diseases; terminal cancer.

Mean age of enrolled patients was 55.4 ± 8.2 years in Gr. 1 and 51.3 ± 10.6 years in Gr. 2, P > 0.5. They were predominantly males, hypertensive, smokers and with lipid disorders (Table 1). The majority of patients were admitted to the hospital within the first 2–4 hours from onset of angina attack and on admission they had electrocardiographic signs of acute myocardial infarction of the left ventricle.

As we can see from Table 1, the studied groups did not differ in main clinical and angiographic characteristics, and significant proportion of patients in both groups had type B2/C

coronary artery lesions (according to ACC/AHA) (Table 2).

Selective coronarography (SC) and endovascular procedures (EVPs) were performed in accordance with generally accepted standard methods. Every surgeon had experience >200 EVPs/year.

The decision to perform MVT was made in case of acute IRA occlusion, after mechanical restoration of the arterial lumen. If coronarography performed after that revealed angiographic signs of thrombus, MVT was done. This procedure was performed by 3–5 slow catheter passages in the area of target lesion. Thereafter, blood flow in the IRA was assessed according to TIMI and MBG classifications, and then the target part of vessel was analyzed using digital computed angiography (Table 2). In the majority of cases, thrombextraction was completed by IRA stenting (69.3%).

The following devices were used for MVT: QuickCat – KenseyNash (16 interventions; 21.3%); Export – Medtronic (18 interventions; 24%), Diver – Invatec (20 interventions; 26.7%); Eliminate – Terumo (21 interventions; 28%). Figure 1 shows brief description of MVT devices.

There are many MVT devices; however, they have in common the following general principles: 1) pre-mounted thin metal stylet ended 2.5 cm from the distal tip of the catheter. As a result, pushability of the device improves and more favorable conditions arise for prevention from its kinking in the difficult segments of coronary arteries; 2) hydrophilic coating of the catheter contributes to its successful passing through the coronary artery; 3) all-metal braided shaft and long monorail part; 4) due to 6–7 Fr catheter diameter, these devices can be used during transradial interventions; 5) the set con-

**Table 2.** Baseline coronarography data from the studied groups

Characteristics	Group 1 (n = 75)	Group 2 (n = 74)	P
Infarct-related artery:			
LAD	30 (40%)	34 (46%)	NS
LCX	8 (10.4%)	8 (10.1%)	NS
RCA	37 (49.6%)	32 (43.9%)	NS
Number of affected arteries	1.5 ± 0.7	1.6 ± 0.8	NS
IRA diameter (mm)	3.3 ± 0.3	3.1 ± 0.4	NS
Lesion length (mm)	17 ± 7	19 ± 5	NS
IRA total occlusion	58 (77.3%)	59 (79.7%)	NS
Morphology of affected vessel (B2/C), %	63 (84%)	64 (86.5%)	NS
Blood flow in the IRA (by TIMI):			
0–1	61 (81.4%)	58 (78.3%)	NS
2–3	14 (18.6%)	16 (21.7%)	NS
Thrombus assessment (by TBG)			
2	12 (16%)	16 (21.6%)	NS
3	24 (32%)	24 (32.4%)	NS
4	18 (24%)	14 (18.9%)	NS
5	21 (28%)	20 (27.1%)	NS

tains a syringe for vacuum creation and filter (for thrombus masses filtration).

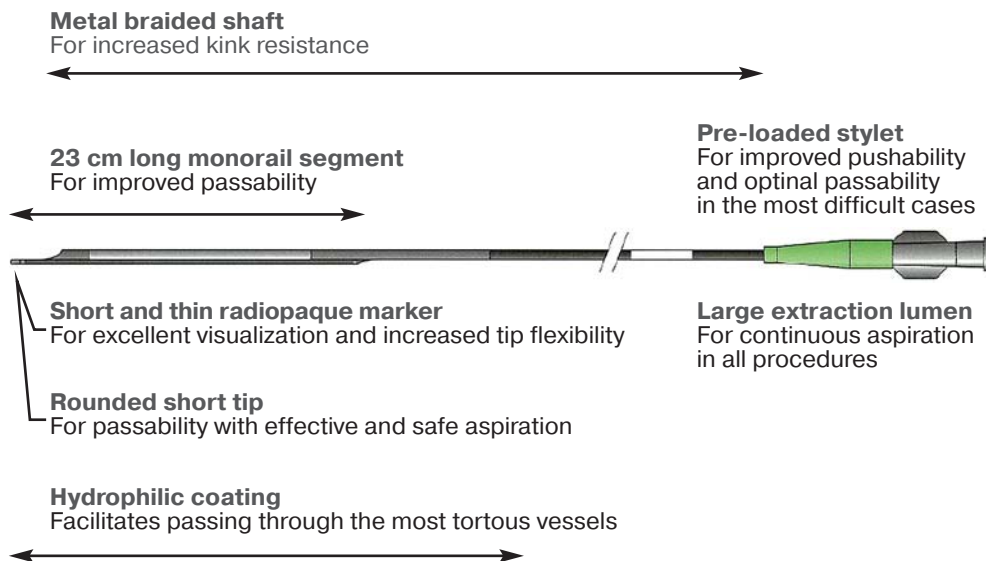
Taking into account an absence of well established standards for assessing thromb-extraction outcomes to date, we used the following criteria: TIMI 2–3 antegrade blood flow (after procedure completion); satisfactory opacification of microcirculatory vessels (MBG 2–3); no signs of thrombus masses dislocation after procedure; no marked dissection or signs of extravasation at the place of previous occlusion.

Prior to the endovascular procedure the patients received acetylsalicylic acid 100 mg, clopidogrel 150 mg followed by daily dose of 75 mg throughout the in-hospital period. The patients with systolic blood pressure higher

than 100 mm Hg received intravenous infusion of nitroglycerine at a dose of 0.25–0.5 µg/kg/min. Intravenous heparin administration was an obligatory condition for thrombus aspiration. Heparin therapy was started as bolus infusion (70 units per kg of body weight) with following drug infusion to achieve activated clotting time (ACT) more than 250 seconds.

After completion of the IRA angioplasty, nitroglycerine 200–400 µg was administrated intracoronary as a bolus and the lesion was assessed using digital computed angiography.

The patients were followed up in the intensive care unit (ICU) within the first day with subsequent transfer to cardiology department. Then, the patients underwent examinations including 24-hour ECG monitoring, heart ultra-

**Fig. 1.** Basic design of catheter for manual vacuum thrombextraction.

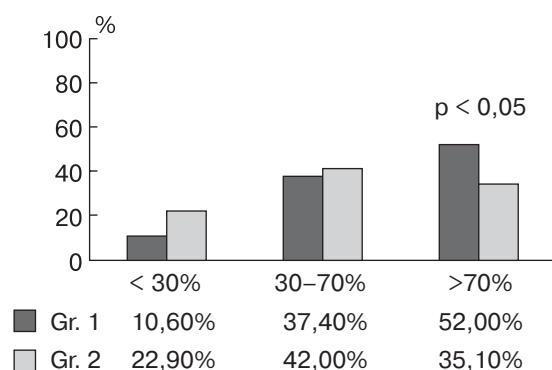
sonography, and on Day 8 cycle ergometry. Mean in-hospital stay duration was  $11.3 \pm 2.9$  days in Gr. 1 and  $10.9 \pm 2.7$  days in Gr. 2 (NS).

## Results

No deaths or recurrent AMI were observed during in-hospital stage in the studied groups. Acute coronary insufficiency accompanied with angina attack and ECG changes was observed in 1 (1.3%) patient from Gr. 1 and 2 (2.7%) patients from Gr.2. In all cases the cause was subacute stent thrombosis. They successfully underwent recanalization followed by balloon angioplasty. At the time of discharge, all studied patients had no angina attacks. By CE data, mean exercise tolerance was  $68.3 \pm 18.5$  W in Gr. 1 and  $65.4 \pm 17.9$  W in Gr. 2. Stress test was positive in 11 patients (14.6%) from Gr. 1 and 13 patients (17.5%) from Gr. 2, respectively (NS). Therefore, statistically insignificant trend towards improved stress test results was observed in Gr.1.

By laboratory data, CPK-MB level on Day 1 was  $166 \pm 22$  U in Gr.1 and  $158 \pm 25$  U in Gr.2, on Day 2 –  $234 \pm 35$  U in Gr.1 and  $239 \pm 37$  U in Gr. 2 (NS). Therefore, there were no significant differences in the size of myocardial infarction using this laboratory data of this cardiospecific enzyme.

Fig. 2 shows that electrocardiographic criterion of more complete ST resolution was observed more often in Gr.1. After EVP completion, ST segment returned completely or partially to the isoelectric line in 39 patients (52%) from Gr. 1, whereas similar pattern was noted in 26 patients (35.1%) from Gr.2 ( $p < 0.05$ ).



**Fig. 2.** ST resolution degree after EVP in the studied patients.

The studied arms did not statistically significantly differ in EVP duration, fluoroscopy time, and consumption of contrast agent (Table 3).

As Table 4 shows, the arms did not significantly differ in parameters of IRA blood flow. Meanwhile, myocardial perfusion according to MBG in Arm 1 was significantly better compared with Arm 2. It should be also noted that balloon angioplasty of the IRA was performed considerably less frequently in Arm 1 (by 22%,  $p < 0.05$ ).

Macroscopically visible thrombus masses were successfully removed in 42 patients (56%) from Gr. 1 (Fig. 3).

It should be noted that optimal angiographic effect was achieved after thrombextraction in 5 patients (6.6%) from Gr. 1, i.e. there was no hemodynamically significant stenosis of the IRA, and as a result no further angioplasty was required (Fig. 4).

Immediate angiographic success was achieved in 94.7% (Gr.1) and 90.5% (Gr.2).

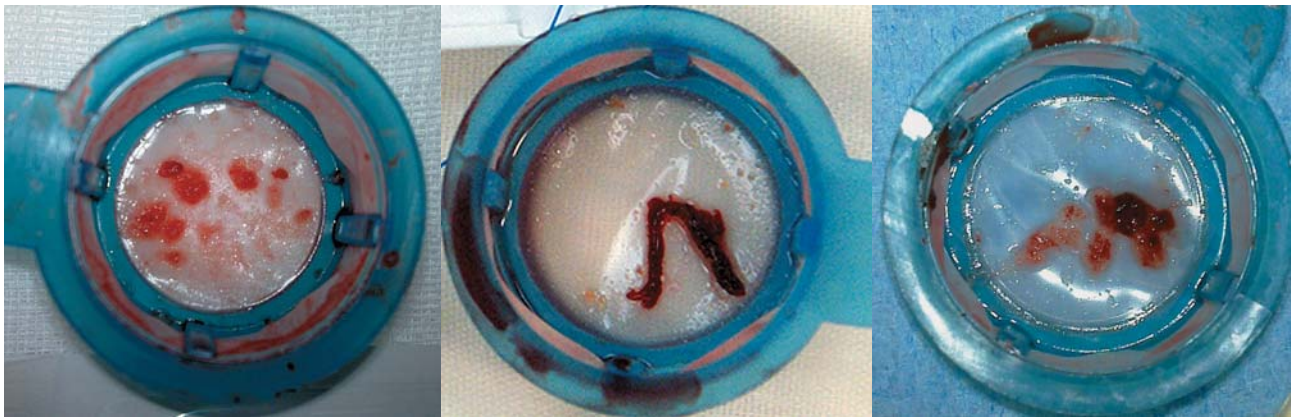
**Table 3.** Mean EVP duration, fluoroscopy time, and consumption of contrast agent

Characteristics	Group 1 (n = 75)	Group 2 (n = 74)	p
Mean procedure duration (min)	$72 \pm 11$	$61 \pm 10$	NS
Mean fluoroscopy time (min)	$18,9 \pm 6,8$	$17,4 \pm 8,1$	NS
Mean consumption of contrast agent (ml)	$239 \pm 56$	$207 \pm 45$	NS

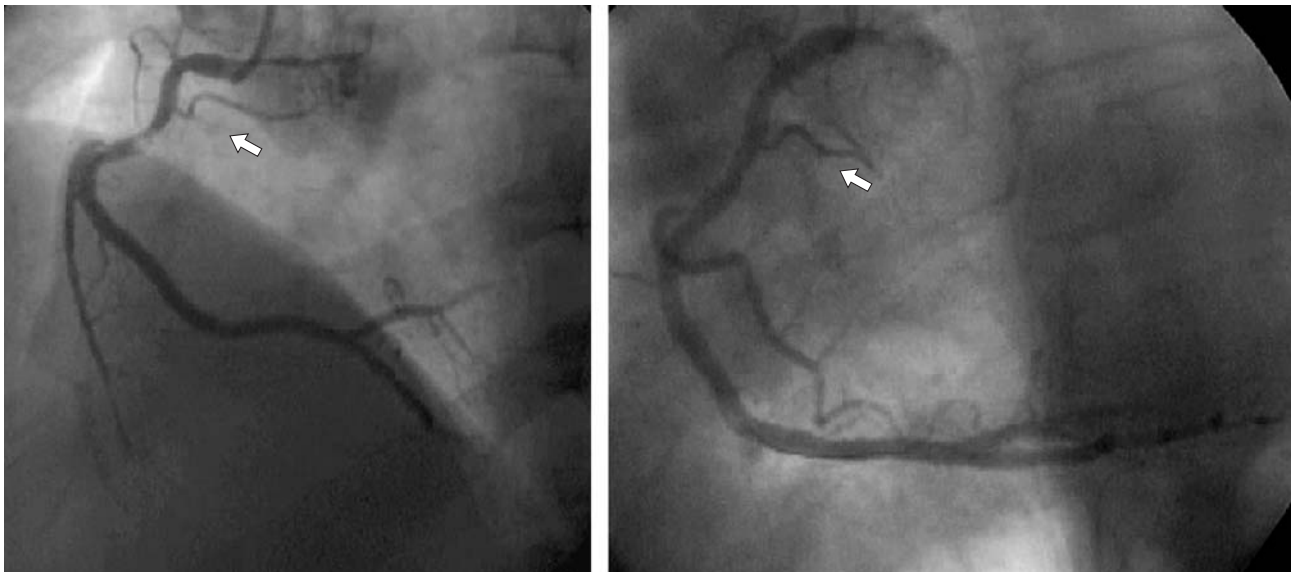
**Table 4.** Immediate coronarography outcomes of the EVPs

Characteristics	Group 1 (n = 75)	Group 2 (n = 74)	p
TIMI			
0/1:	2 (2.6%)	3 (4.1%)	NS
2:	11 (14.8%)	6 (8.1%)	NS
3:	62 (82.6%)	66 (87.8%)	NS
MBG			
0/1:	3 (4%)	14 (18.9%)	$p < 0.05$
2:	21 (28%)	26 (35.1%)	NS
3:	51 (68%)	34 (46%)	$p < 0.05$
Balloon predilatation (%)	40%	62.1%	$p < 0.05$





**Fig. 3.** Thrombus masses removed during thrombectomy from the IRA in patients from Gr.1.



**Fig. 4.** Coronary angiogram of a patient with acute myocardial infarction. On the left figure, angiographic signs of thrombus in the RCA can be seen, on the right figure, RCA angiogram of the same patient after thrombectomy.

Among complications in Gr.1, there should be noted one case of “no-reflow” phenomenon, one additional case of acute in-stent thrombosis (4 hours after EVP) and two cases of distal embolization. In Gr. 2, two cases of “no-reflow” phenomenon and acute in-stent thrombosis each and 3 cases of distal embolization of the IRA were observed. There were no significant differences between the arms in EVP-related serious morbidity (Table 5). All acute in-stent thrombosis cases were successfully resolved by repeat PTCAs.

### Discussion and conclusions

The studies intended to use a new device for treatment of a specific disease should answer some important questions, including the most significant: efficacy of an option and device used for treatment of this pathology, its safety and, equally important, cost efficiency. This study has demonstrated clearly enough that manual vacuum thrombectomy in combination with angioplasty of the infarct-related artery is slightly more effective than angioplasty alone based on blood flow restoration in the

**Table 5.** Angiographic morbidity in the studied arms

Characteristics	Group 1 (n = 50) (thrombectomy)	Group 2 (n = 74) (control)	p
“No-reflow”	1 (1.3%)	2 (2.7%)	NS
Distal embolization after the EVP	2 (2.6%)	3 (4.1%)	NS
Acute in-stent thrombosis	1 (1.3%)	2 (2.7%)	NS
Total number of complications	4 (5.3%)	7 (9.5%)	NS



IRA in comparable AMI patients. Firstly, thrombus masses were removed completely or partially using thrombextraction in 56% cases; therefore, probability of thrombus masses dislocation in the IRA was considerably reduced. Secondly, complete ST resolution was observed significantly more frequently after intervention (52%) compared with the control arm (35.1%). MVT efficacy is confirmed by better microcirculatory and myocardial perfusion parameters in this respective arm compared with the control arm after thrombextraction combined with angioplasty. MBG-3 was observed in 68% and 46% of cases in the Gr. 1 and Gr. 2, respectively. Thirdly, both to achieve optimal results and to prepare for further stenting, balloon angioplasty was required significantly more rarely in Gr. 1. Importantly, optimal angiographic results were achieved in Gr. 1 after thrombextraction and no balloon angioplasty or stenting was required in some cases (6.6%). Additionally, cost efficiency of the intervention was considerably reduced, i.e. relevant economic effect is seen. However, in-hospital mortality rates, AMI relapse rates, and IRA thrombosis rates did not significantly differ between the studied arms. No significant prolongation of the intervention duration was observed in Arm 1 compared with Gr. 2. Clinical courses of disease at in-hospital stage, morbidity and mortality rates did not significantly differ between the arms. Therefore, we conclude that MVT is quite safe to remove thrombus masses from the IRA and effective enough for both thrombus evacuation and adequacy of blood flow restoration in the infarct-related artery. However, further experience and thorough comparative analysis of obtained results are required to definitely determine a role of this option in endovascular treatment of AMI patients.

## References

1. Iosseliani D.G., Filatov A.A., Rogan S.V. et al. Blood flow restoration in infarct-related coronary artery in acute myocardial infarction: effective or just spectacular? *International Journal of Interventional Cardioangiology*, 2003, 1, 33.
2. Van't Hof A., Liem A., Syapranata H. et al. Angiographic assessment of myocardial reperfusion in patients treated with primary angioplasty for acute myocardial infarction. *Circulation*, 1998, 97, 2302–2306.
3. Keeley E.C., Boura J.A., Grines C.I. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet*, 2003, 361, 13–20.
4. Eeckhout E., Kern M.J. The coronary no-reflow phenomenon: a review of mechanisms and therapies. *Europ. Heart J.*, 2001, 22, 729–739.
5. Shah P. Distal Embolization After Percutaneous Coronary Interventions. *J. Am. Coll. Cardiol.*, 2007, 50 (17), 1647–1648.
6. The TIMI Study Group: Special report: The Thrombolysis in Myocardial Infarction (TIMI) Trial. *New Engl. J. Med.*, 1985, 312, 932–936.
7. Antman E.A., Cohen M., Bernink P. et al. The TIMI Risk Score for Unstable Angina/Non-ST Elevation MI. *JAMA*, 2000, 284, 835–842.
8. Napodano M., Ramondo A., Tarantini G. et al. Predictors and time-related impact of distal embolization during primary angioplasty. *Eur. Heart J.*, 2009, 30, 305–313.
9. Lablanche J.M., Fourrier J.L., Gommeaux A. et al. Percutaneous aspiration of a coronary thrombus. *Catheter. Cardiovasc. Diagn.*, 1989, 17, 97–98.
10. Svilaas T., Vlaar P.J., van der Horst I.C. Thrombus aspiration during primary percutaneous coronary intervention. *New Engl. J. Med.*, 2008, 358, 557–567.
11. Silva-Orrego P., Colombo P., Bigi R. Thrombus aspiration before primary angioplasty improves myocardial reperfusion in acute myocardial infarction: the DEAR-MI (Dethrombosis to Enhance Acute Reperfusion in Myocardial Infarction) study. *J. Amer. Coll. Cardiol.*, 2006, 17, 48(8), 1552–1559.
12. Sardella G., Mancone M., Bucciarelli-Ducci C. Thrombus aspiration during primary percutaneous coronary intervention improves myocardial reperfusion and reduces infarct size: the EXPIRA (thrombectomy with export catheter in infarct-related artery during primary percutaneous coronary intervention) prospective, randomized trial. *J. Am. Coll. Cardiol.*, 2009, 53, 309–315.
13. Tsvetkov H., Mosseri M. Myocardial Blush Grade: An Interventional Method for Assessing Myocardial Perfusion. *IMAJ*, 2008, 10, 465–467.
14. Schroder R., Dissmann R., Bruggemann T. et al. Extent of early ST segment elevation resolution: a simple but strong predictor of outcome in patients with acute myocardial infarction. *J. Am. Coll. Cardiol.*, 1994, 24, 384–391.
15. Sianos G., Papafakis M.I., Serruys P.W. et al. Angiographic thrombus burden classification in patients with ST-segment elevation myocardial infarction treated with percutaneous coronary intervention. *J. Invasive Cardiol.*, 2010, 22 (10 Suppl B), 6B–14B.

# Left Main Coronary Artery Stenting in Patients with Various Types of Coronary Heart Disease: Immediate and Mid-Term Results

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*The lesions of the left main coronary artery are found in 10,9% of patients with various forms of coronary heart disease. The authors describe immediate results of examination and treatment of 134 patients with various forms of CHD who underwent LMCA endovascular interventions in the Moscow City Center of Interventional CardioangiologY from June 2002 to February 2012. All endovascular interventions on the LMCA were successful. In 8,01 ± 2,1 months after stenting of the LMCA repeated examination was conducted in 97 (72,4%) patients with previously implanted bare metal and drug-eluting stents. Control coronary angiography was performed in 97 patients with 112 stents, including 57 DES (50,9%) and 55 (BMS 49,1%). Total rate of restenosis after stenting of the LMCA was 37,5% (n = 42). In the group of patients with previously implanted DES the rate of restenosis was 21,05% (n = 12), while in patients with BMS – 54,5% (n = 30). Our results are suggestive of relative effectiveness of the method of LMCA stenting.*

**Key words:** lesion of the LMCA, stenting of the LMCA, immediate and late results.

Selective coronarography shows that the left main coronary artery (LMCA) lesion is observed in 10.9% of patients with various types of coronary heart disease (1–2). Early diagnostics and use of the most rational treatment options in this patient population is currently one of the most important objectives, as delay in treatment is associated with poor clinical prognosis and high early mortality. In patients with LMCA lesion on medication therapy, 24-, 36-, and 42-month mortality rate was 43.6%, 51.1%, and 73.6%, respectively (19).

Given such unsatisfactory prognosis associated with the medication therapy, the clinicians have started to use different myocardial revascularization methods for this disease over the last decade. Initially, coronary artery bypass grafting was the most widely used procedure for myocardial revascularization, and until recently, it was a basic and, possibly, a single treatment option. However, this population has recently become more numerous, and coronary stenting is more frequently used as a treatment option (3–18). Especially, it is related to geriatric patients, subjects with very severe left

ventricular dysfunction, those who previously underwent direct myocardial revascularization surgeries, and persons with concomitant severe diseases etc. If indication for LMCA stenting is correctly determined, the improved clinical status and functional capability of the left ventricle are observed in the vast majority of patients. However, in-stent stenosis and late drug-eluting stent thromboses are considerable limitations for wider introduction of stenting in treatment of subjects with LMCA lesions (2, 16, 18). Many investigators report this, but their opinions are contradictory. Only further investigation of immediate and long-term results of LMCA stenting with up-to-date stents will determine actual efficacy of endovascular treatment for stenosed/occluded LMCA lesions.

The objective of this study was to assess immediate and mid-term clinical and angiographic results of LMCA stenting in patients with various types of CHD.

The indication for endovascular LMCA intervention was angiographically and clinically significant stenosis of LMCA involving and not involving its branch orifices. Endovascular interventions were generally performed in patients with high risk of CABG.

All patients were examined according to well-established cardiovascular practice including detailed history, ECG, 24-hour ECG monitoring, EchoCG, stress test (unless contraindicated) to determine exercise tolerance, left ventriculography, and selective coronarography.

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## Material and methods

The study included 134 patients with various types of CHD who underwent LMCA endovascular interventions in the Moscow City Center of Interventional Cardioangiography from June 2002 to February 2012.

Clinical and historical characteristics of studied patients are presented in Tables 1–2.

**Table 1.** Clinical characteristics of patients

Males	64.2% (n = 86)
Mean age	62.4 ± 10.1 years
CHD duration	5.6 ± 0.4 years
Diabetes mellitus	14.2% (n = 19)
Essential arterial hypertension	85.1% (n = 114)
Dyslipidemia	70.9% (n = 95)
History of MI	47.8% (n = 64)
Previous CABG	19.4% (n = 26)
Peripheral artery disease:	
brachiocephalic	
atherosclerosis	16.4% (n = 22)
lower limb artery	
atherosclerosis	11.9% (n = 16)
Rhythm and conduction disturbances	9% (n = 12)
Chronic renal insufficiency	4.5% (n = 6)
History of CVA	6.7% (n = 9)

**Table 2.** History data of patients

<b>Diagnosis at the moment of the first admission to the hospital</b>	
Acute CHD:	52.2% (n = 70)
progressive angina	8.2% (n = 11)
AMI	44% (n = 59)
Chronic CHD (effort angina of various functional classes)	47.8% (n = 64)
Clinical signs of heart failure	9% (n = 12)
IABP	4.5% (n = 6)

**Table 3.** 24-hour ECG monitoring (n = 134) and stress test (n = 90) results

Mean LVEF	54 ± 4.6%
24-hour ECG monitoring (n = 134)	
ischemic ECG changes	24% (n = 32)
Stress test (n = 61):	
positive	67.2% (n = 61)

**Table 4.** Baseline angiographic characteristics of LMCA lesions

LMCA stenosis	55–100% (mean 79.4 ± 4.8%)
Isolated LMCA lesion	3.7% (n = 5)
Ostial LMCA lesion	35.8% (n = 48)
LMCA trunk lesion	21.6% (n = 29)
LMCA bifurcation lesion	42.5% (n = 57)
LMCA acute occlusion	8.2% (n = 11)

Most patients were males (64.2% (n = 86)) aged from 43 to 80 years (mean age 62.4 ± 10.1 years). Mean CHD duration was 5.6 ± 0.4 years. The most common CHD risk factors were essential arterial hypertension, dyslipidemia, smoking (see Table 1). A history of myocardial infarction was in 47.8% of patients (n = 64). 52.2% of patients (n = 70) were admitted to the hospital by ambulance with clinical signs of progressive angina or at early stages of acute myocardial infarction.

Rhythm and conduction disturbances were observed in 9% of cases (n = 12). Clinical signs of acute heart failure were observed in 10.5% of subjects (n = 14), hence intra-aortic balloon pump (IABP) had to be used in some cases (4.5%, n = 6). Among them, 47.8% (n = 64) of patients had chronic CHD and 52.2% (n = 70) of patients had acute CHD: 8.2% patients (n = 11) had acute myocardial infarction, 44% patients (n = 59) had progressive angina.

EchoCG was performed in all patients to assess left ventricle ejection fraction (mean LVEF was 54 ± 4.6%). Exercise stress test was performed unless contraindicated. Due to contraindications, exercise stress test was not performed in 44 patients (32.8%). Among the remaining patients from the study arm, 67.2% of subjects (n = 61) had positive stress test results. Mean exercise tolerance threshold was 56.5 ± 2.4 W (Table 3).

Coronarography was performed urgently for unstable clinical status in 17.2% patients (n = 23). Mean degree of LMCA stenosis was 79.4 ± 4.8%. During coronarography, acute LMCA occlusion without intersystem collateral filling was identified in 8.2% of patients (n = 11). Isolated LMCA lesion was observed in 3.7% of cases (n = 5). Ostial LMCA lesions and LMCA trunk lesions were revealed in 35.8% (n = 48) and 21.6% of cases (n = 29), respectively. LMCA bifurcation lesions involving larger LCA branches were observed most frequently (42.6%, n = 57). The majority of patients (86.4%) had hemodynamically significant changes in other coronary arteries. Table 4 shows baseline angiographic characteristics of LMCA lesions.

## Results

All patients had successful endovascular interventions. Various methods of endovascular interventions were chosen depending on localization of LMCA lesion. When ostial LMCA lesions were stented, direct stenting was used in the majority of cases (86.7%). In case of distal, LMCA bifurcation lesion involving athero-

**Table 5.** Stenting of the left main coronary artery

LMCA mechanical recanalization	8.2% (n = 11)
LMCA balloon angioplasty followed by stenting	10.5% (n = 14)
LMCA direct stenting	89.6% (n = 120)
LMCA kissing/V-stenting	19.4% (n = 26)
LMCA stenting involving LAD orifice	14.2% (n = 19)
LMCA stenting involving LCX orifice	9% (n = 12)
Type of implanted stent	
1 in total, 134 patients received 139 stents; out of them 1 stent was implanted in 129 patients (96.3%), while 2 stents – in 5 patients (3.7%)	
Bare metal stent	41.7% (n = 58)
Drug-eluting stent (anti-proliferative, anti-thrombotic coating)	58.3% (n = 81)
Mean stent diameter, mm	3.32 ± 0.36
Mean stent length, mm	14.1 ± 1.5
Mean pressure of stent implantation, atm.	16.5 ± 1.45
Mean time of stent implantation, sec.	18.2 ± 2.4
Simultaneous intervention involving:	
1 vessel	26.9% (n = 36)
2 vessels	55.2% (n = 74)
3 vessels	17.9% (n = 24)

sclerotic LCX orifice, distal part of LMCA was predilated with introducing the balloon through LCX orifice. Then, LMCA was stented involving LCX orifice; in some cases of distal LMCA lesions, the distal one-third of LMCA was stented with further stenting of LCX orifice through meshes of the LMCA stent (debulking). When atherosclerotic process was spread to LAD orifice, LMCA was stented involving LAD orifice. Kissing/V-stenting or T-stenting was performed in case of more complex LMCA bifurcation lesions when large branches (LAD and LCX) were involved (Table 5).

Drug-eluting stents with antiproliferative and antithrombotic coating were implanted in LMCA more frequently (58.3%, n = 81). In the remaining patients, so-called bare metal stents were implanted. Five patients (3.7%) had 2 stents each implanted in LMCA. Good immediate angiographic results were achieved in 100% of cases. All LMCA endovascular interventions were uncomplicated. In-hospital period was uncomplicated in 96.3% of cases (n = 129), these patients were discharged in stable condition. In-hospital mortality was 3.7% (n = 5). All deceased patients had acute CHD; causes of death were progression of acute left ventricular failure, various rhythm and conduction disturbances.

### Mid-term results of the LMCA stenting

Ninety seven patients (72.4%) with bare metal stents and drug-eluting stents previously implanted in LMCA were re-examined  $8.01 \pm 2.1$

months after LMCA stenting. One patient (0.8%) died from renal cancer. In re-examined patients, recurrence of clinical angina was observed on average 3.4 months after LMCA stenting and was caused, in general, by LMCA in-stent stenosis. Effort angina of various functional classes was observed in 41.2% (n = 40) of cases; 18 patients (18.6%) were re-admitted with acute CHD, 16 patients (16.4%) out of them had progressive angina and 2 patients had acute myocardial infarction (2.1%) caused by LMCA in-stent stenosis. Among re-examined patients, 40.2% (n = 39) were asymptomatic. In mid-term period, 16.5% patients (n = 16) had clinical signs of heart failure. Mean LVEF was  $50.2 \pm 2.4\%$  when myocardial contractility was examined in the mid-term period after LMCA stenting. Additionally, exercise tolerance significantly increased from  $56.5 \pm 2.4$  W to  $75 \pm 3.6$  W ( $p < 0.05$ ). There were 31.4% (n = 21) of positive exercise stress test results. Based on the mid-term results, acute and chronic CHD, clinical signs of heart failure, and ischemic ECG changes during 24-hour ECG-monitoring and exercise stress test are observed more frequently in patients with previously implanted LMCA bare metal stents as compared with drug-eluting stents (Table 6).

During control coronarography in 97 patients, 112 stents were assessed: out of them, 57 stents (50.9%) were drug-eluting and 55 (49.1%) were bare metal. Overall restenosis after LMCA stenting was 37.5% (n = 42). Restenosis in patients with previously implant-



**Table 6.** Data of mid-term examinations

	All patients (all stents)	BMS*	DES**
<b>Diagnosis at the moment of re-admission to the hospital:</b>			
Acute CHD:	18.6% (n = 18)	12.4% (n = 12)	6.2% (n = 6)
Progressive angina	16.4% (n = 16)	12.4% (n = 12)	4.1% (n = 4)
AMI	2.1% (n = 2)	2.1% (n = 2)	–
Effort angina of various functional classes	41.2% (n = 40)	29.9% (n = 29)	10.3% (n = 10)
Asymptomatic patients	40.2% (n = 39)	13.4% (n = 13)	26.8% (n = 26)
Overall mortality	0.8% (n=1)	0.8% (n = 1)	–
Clinical signs of heart failure	16.5% (n = 16)	14.4% (n = 14)	2.1% (n = 2)
Mean LVEF		50.2 ± 2.4%	
24-hour ECG monitoring (n = 134) ischemic ECG changes	18.6% (n = 18)	12.4% (n = 12)	6.2% (n = 6)
Stress test (n=72): positive	31.9% (n = 23)	22.2% (n = 16)	9.7% (n = 7)

\*BMS – bare metal stent, \*\*DES – drug-eluting stent.

ed drug-eluting stents and patients with previously implanted bare metal stents was 21.05% (n = 12) and 54.5% (n = 30), respectively. Such high restenosis degree in stents previously implanted in the LMCA is likely due to LMCA baseline features (LMCA contains more elastic tissue compared with other parts of coronary arteries). Application of drug-eluting stents significantly reduced restenosis rate after LMCA stenting.

Medication therapy in mid-term period after LMCA stenting was recommended for 23.8% (n = 10) of patients. Repeated endovascular intervention (balloon angioplasty) for LMCA in-stent stenosis was performed in 47.6% (n = 20) of subjects, with good immediate angiographic results; CABG was recommended for 12 patients (28.6%).

Discussion. The conducted study demonstrated that the vast majority of patients with LMCA stenosis had good immediate stenting results using both bare metal stents and drug-eluting stents (100%). Good immediate angiographic results were achieved in all patients when LMCA was stented; patients with progressive angina became stable and patients with acute myocardial infarction had smoother clinical course. Only patients with severe disturbances of left ventricular functional capacity resulted from acute myocardial infarction (progressive acute left ventricular insufficiency, fatal rhythm disturbances) had unfavorable outcomes. Lee SW et al. (5) obtained similar results, immediate angiographic success of LMCA stenting was 94% (n = 17), in-hospital mortality rate was 11% (n = 2). Park et al. (6) reported 100% immediate success when patients with hemodynamically significant LMCA lesions

were stented; there were no in-hospital complications (in-stent thrombosis, fatal Q-wave myocardial infarction, urgent CABG). Lee BK et al. (14) published the similar results: angiographic success of stenting was 99.5%, there was no in-hospital deaths in patients under study. Early in-hospital mortality rate in our study was 3.7% (n = 5), no repeated endovascular or surgical interventions were required.

In mid-term period after LMCA stenting, clinical and functional status of patients was evaluated and control coronarography was performed to assess the target segment of coronary artery. The study demonstrated more "benign" clinical course of underlying disease: 40.2% of re-examined patients were asymptomatic, 2 patients (2.1%) had acute myocardial infarction due to LMCA in-stent restenosis. When myocardial contractility and exercise tolerance were examined in our study, we observed insignificant mean increase of LVEF in mid-term period after LMCA stenting up to 50.2 ± 2.4% and significant increase in exercise tolerance from 56.5 ± 2.4 W up to 75 ± 3.6 W (p < 0.05). In the majority of cases, the reoccurrence of angina pectoris was caused by LMCA in-stent restenosis. B.K. Lee et al. (14) concluded that total LMCA in-stent restenosis in 6 month after LM stenting was 33,3%. Carrie et al. (11) received similar results: 9 months after LMCA stenting using bare metal stents, in-stent stenosis was observed in 29.8% of cases; myocardial infarction developed in 5.1% of cases; repeated LMCA interventions were performed in 22.8% of cases due to in-stent stenosis. In our study, in mid-term period after LMCA stenting repeated LMCA interventions were performed in 47.6% (n = 20) of cases due to LMCA



in-stent restenosis; CABG was recommended for 12 patients (28.6%). It should be noted that the percentage of bare metal and drug-eluting stent restenosis was 54.5% ( $n = 30$ ) and 21.05% ( $n = 12$ ), respectively; hence, an advantage of drug-eluting stents for LMCA lesions is demonstrated.

## Conclusion

The obtained results demonstrated the relative efficacy of LMCA stenting. However, further development of the most optimal and scientifically reasonable approaches to the treatment of such difficult coronary lesions as LMCA stenosis, is a top priority to extend indications for LMCA stenting and to use this option not only in patients with contraindicated surgical treatment, but also in patients with stable angina.

## References

1. Park S.J., Park S.W. Hong M. et al. Long-term (three-year) outcomes after stenting of unprotected left main coronary artery stenosis in patients with normal left ventricular function. *Am. J. Cardiol.*, 2003, 91, 12–16.
2. Chieffo A., Orlic D., Airolidi F. Early and mid-term results of Cypher stents in unprotected left main. *J. Am. Coll. Cardiol.*, 2004, 43, 5, 1116–1118.
3. Black A., Cortina R., Bossi I. et al. Unprotected left main coronary artery stenting: correlates of midterm survival and impact of patient selection. *J. Am. Coll. Cardiol.*, 2001, 37, 382–388.
4. Buszman P., Zurakowski A., Banasiewicz-Szkrobka I. et al. Percutaneous Transluminal Coronary Angioplasty of unprotected left main coronary artery in patient with severe left ventricular contractility dysfunction. *Kardiol. Pol.*, 2006, 64 (9), 1018–1020.
5. Lee S.W., Hong M.K., Lee C.W., et al. Early and late clinical outcomes after primary stenting of the unprotected left main coronary artery stenosis in the setting of acute myocardial infarction. *Int. J. Cardiol.*, 2004, 97 (1), 73–76.
6. Park S.J., Lee C.W., Kim Y.H., et al. Technical feasibility, safety, and clinical outcome of stenting of unprotected left main coronary artery bifurcation narrowing. *Am. J. Cardiol.*, 2002, 90(4), 374–378.
7. Kosuga K., Tamai H., Kyo E. et al. Role of new devices for angioplasty in the unprotected left main coronary artery. *J. Cardiol.*, 2001, 38 (5), 245–253.
8. Lee R.J., Lee S.H., Shyu K.G. et al. Immediate and long-term outcomes of stent implantation for unprotected left main coronary artery disease. *Int. J. Cardiol.*, 2001, 80 (2–3), 173–177.
9. Lopez-Palop R., Pinar E., Saura D. et al. Short- and medium-term outcomes of percutaneous coronary intervention for unprotected left main coronary artery disease in patients who are poor candidates for surgical revascularization. *Rev. Esp. Cardiol.*, 2004, 57(11), 1009–1013.
10. Marti V., Planas F., Cotes C. et al. Immediate and long-term outcome after angioplasty with stenting of the left main coronary artery. *Rev. Esp. Cardiol.*, 2004, 57 (11), 1009–1013.
11. Carrie D., Maupas E., Hmem M. et al. Clinical and angiographic outcome of stenting of unprotected left main coronary artery bifurcation narrowing. *Int. J. Cardiovasc. Intervent.*, 2005, 7 (2), 97–100.
12. Sakai K., Nakagawa Y., Kimura T. et al. Primary angioplasty of unprotected left main coronary artery for acute anterolateral myocardial infarction. *J. Invasive Cardiol.*, 2004, 16я(11), 621–625.
13. Park S.J., Hong M.K., Lee C.W. et al. Elective stenting of unprotected left main coronary artery stenosis: effect of debulking before stenting and intravascular ultrasound guidance. *J. Am. Coll. Cardiol.*, 2001, 38 (4), 1054–1060.
14. Lee B.K., Hong M.K., Lee C.W. et al. Five-year outcomes after stenting of unprotected left main coronary artery stenosis in patients with normal left ventricular function. *Int. J. Cardiol.*, 2007, 115 (2), 208–213.
15. Silvestri M., Barragan P., Sainsous J. et al. Unprotected left main coronary artery stenting: immediate and medium-term outcomes of 140 elective procedures. *J. Am. Coll. Cardiol.*, 2000, 35 (6), 1551–1553.
16. Valgimigli M., van Mieghem C.A., Ong A.T. et al. Short- and long-term clinical outcome after drug-eluting stent implantation for the percutaneous treatment of left main coronary artery disease: insights from the Rapamycin-Eluting and Taxus Stent Evaluated At Rotterdam Cardiology Hospital registries (RESEARCH and T-SEARCH). *Circulation*, 2005, 111 (11), 1383–1399.
17. Peszec-Przybula E., Buszman P., Bialkowska B., Zurakowski L. Stent implantation for the unprotected left main coronary artery. The long-term outcome of 62 patients. *Kardiol Pol.* 2006; 64 (1); 1–6.
18. Chieffo A., Stankovich E., Binizzoni E. et al. Early and mid-term results of drug-eluting stents implantation in unprotected left main. *J. Am. Coll. Cardiol.*, 2005, III (6), 791–795.
19. Cohen M.V., Gorlin R. Main left coronary artery disease. Clinical experience from 1964-1974. *Circulation*, 1975, 52, 275–285.

# First Experience of Altay Regional Cardiology Dispensary with the Use of Femoral Puncture Access Site Closure Devices During Radiosurgical Interventions

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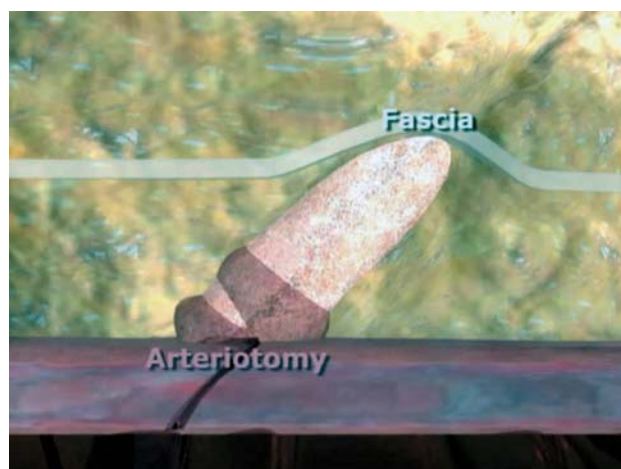
Altay Regional Cardiology Dispensary, Barnaul, Russia

*Each year the number of endovascular interventions is continuously growing. Since endovascular interventions are invasive methods of treatment, sometimes different complications occur at the puncture site: hematomas, arteriovenous fistulas, pulsatile hematomas which worsen the patient's condition and require various measures for their liquidation. In Altay Territory Cardiology Dispensary, different devices for closure of puncture apertures in the femoral artery are used. Closure devices demonstrated their efficacy and safety in preventing complications, especially in patients at risk. However, the use of any closure device in different categories of patients requires further investigation and accumulation of experience.*

**Key words:** puncture aperture, Exoseal, Angio-seal, hemostasis, pulsatile hematoma.

## Introduction

**Background.** Method of radioangiography is widely used in modern medicine for diagnostics and treatment of cardiovascular diseases (1, 2, 4). Due to its high informativity, this method is widely recognized and it became a so called "gold standard" (2, 4). However, as it is an invasive method of investigation, such complications as hematomas, thromboembolism, arteriovenous fistulas as well as development of postangiographic pulsatile hematomas and pseudoaneurysms of peripheral vessels are expected, which account for 0.2% – 10–15% from a total number of iatrogenic pseudoaneurysms according to the data of different authors (1, 4, 5). After conduction of diagnostic angiography, percentage of complications is smaller (0.2–0.5%) then after surgical manipulations (2–15%) (2, 3, 5). Age older than 60 years, female sex, obesity, simultaneous cannulation of the artery and the vein, as well as previous diseases of peripheral arteries are registered among risk factors of pseudoaneurysm development (1, 2, 3). In the last years, devices for mechanic closure of femoral artery puncture site have been developed.



**Fig. 1.** Location of plug relative to the vascular wall and fascia.

However, until recently the issues of safety and efficacy of their use as well as their usability by the experts in the field of endovascular treatment remain topical. Objective of this study was to assess new vascular closure devices Exoseal (Cordis) and Angio-Seal Evolution (St. Jude Medical).

The Exoseal Vascular Closure Device is indicated for femoral artery puncture site closure; it reduces the time to hemostasis and ambulation of patients after diagnostic or therapeutic procedures and decreases the number of complications. The Exoseal Vascular Closure Device consists of a plug applicator and an absorbable plug. The plug applicator consists of a handle assembly and a delivery shaft. The absorbable plug is fully enclosed in the distal portion of the delivery shaft (Fig. 1). The plug applicator posi-

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tions and deploys the absorbable plug to the extravascular surface of the femoral artery access site through the existing separate 7F introducer with a working length of up to 12 cm without the need for introducer replacement before use. Hemostasis is achieved when the absorbable plug is deposited on top of arteriotomy site. The plug exhibits partial to advanced absorption at 30 days, with complete absorption between 60 and 90 days post-implant (Fig. 2). The Exoseal plug is MRI compatible.

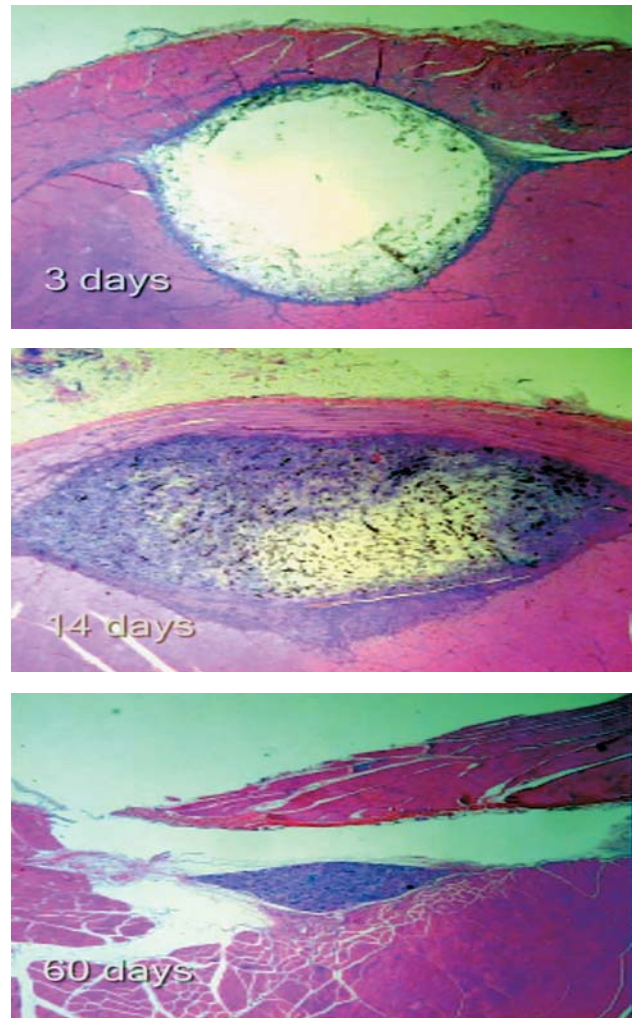
#### **Angio-Seal Evolution device**

Device seals the arteriotomy site by closing it from both sides between two main parts of the device – anchor and collagen seal. Hemostasis is primarily achieved mechanically by compressing the arteriotomy aperture between the anchor and the seal and additionally is increased by collagen ability to stimulate blood coagulation (Fig. 3).

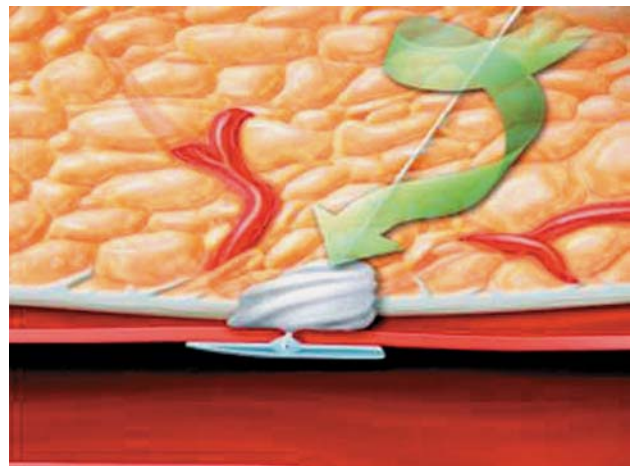
#### **Material and methods**

The Exoseal Vascular Closure Device has been used for 4 months. 100 patients after endovascular treatment procedure with the puncture site closed using this device were enrolled in the study. Femoral artery was closed right after the completion of stenting procedure, sometimes on the next day regardless of the results of last determination of activated partial thromboplastin time. Compression bandage was applied at the puncture site for 12 hours. (Earlier, without using the closure device, a tight compression bandage was applied for 24 hours). On the next day, all patients underwent duplex scanning of lower limb vessels after using the closure device. 40 subjects from a general group of patients weighed over 110 kg, 20 patients weighed 90–110 kg, and 40 patients weighed less than 90 kg. Upper limit of blood pressure ranged from 100 to 180 mm Hg. Success rate for using the system was 98%. In a group of patients weighing over 110 kg there were no complications; one patient (1%) had hematoma (in a group of patients weighing less than 90 kg), however, no special treatment was required; hematoma formed in one more patient (1%) after bed rest violation (long-term psychomotor agitation), no special treatment was required. A total number of complications was 2%.

Angio-Seal Evolution device was used in 40 patients after elective endovascular procedures (Fig. 4). Right after manipulation, the



**Fig. 2.** Histological picture of the plug on Day 3, 14 and 60 after using a closure device.



**Fig. 3.**





**Fig. 4.** Location of the plug according to the duplex scanning data the next day after the Exoseal installation.

post-puncture aperture was closed by the device under X-ray control (X-ray control is recommended to determine the place where the introducer is located in the vessel). Compression bandage in this case was not applied (it is contraindicated when using this device). In 2 hours after endovascular intervention the patient was allowed to get up and walk. In a group of patients where the device was used the weight was 80–110 kg; there were 25 female and 15 male subjects. On the next day,

all patients underwent duplex scanning of lower limb vessels after using Angio-Seal Evolution: no defect in the vascular wall at the puncture site, no data of pseudoaneurysm formation were registered.

Success rate of using Angio-Seal Evolution device was 100%. The number of complications was 0%.

## Conclusion

The incidence of complications after endovascular interventions with femoral approach is reducing with accumulation of experience gained from using Exoseal (Cordis), Angio-Seal Evolution (St. Jude Medical) devices. However, the use of these devices has its advantages and disadvantages. For example, Exoseal has a simpler installation technique as compared with Angio-Seal Evolution, it does not require X-ray control, special storage conditions and has a long-term storage period. However, it is necessary to apply compression bandage after procedure at the manipulation site; it is hard to determine location of the plug right after conducting the procedure. When using Angio-Seal Evolution, X-ray control is required to identify introducer in the artery (it is recommended); the device should be kept in the refrigerator and its storage period is rather short. However, the use of Angio-Seal Evolution allows the patient to ambulate after device implantation in 20 minutes, to be discharged from the in-patient department if there are no other complications in 1 hour (according to the instruction on application), compression bandage after procedure is not applied, in 60–90 days all device components are completely absorbed and dissolved.

According to our data, the use of both closure devices results in decreased number of complications after endovascular procedures; however, it is necessary to continue studies on devices to determine in which case is better to use Angio-Seal Evolution and in which – Exoseal. Of special interest is an experience of using closure devices in a group of patients at high risk of complications (weight greater than 110 kg, female sex, in patients with long-term presence of introducer in the femoral artery, with long-term anticoagulant therapy), who suffer from severe painful sensations caused by compression bandage which may be ineffective. The further use of Exoseal and Angio-Seal Evolution closure devices makes it possible to gain more experience and to reduce the number of complications.

Therefore, as compared with conventional manual hemostasis, closure devices let patients be active significantly earlier after endovascular treatment with lesser number of complications.

## References

1. A.V. Gavrilenko, G.V. Sinyavin. Treatment of false iatrogenic arterial aneurysms. *Angiologia I sosudistaya khirurgia*, 2005, 11, 3. 135–138. (in Russian)
2. Grishin I.N., Savchenko A.N. *Clinical angiology and angi-surgery*. Minsk, Vysheyshaya shkola publishers, 1981, 203 p. (in Russian)
3. Spiridonov A.A., Tutov I.G., Pryadko S.I. et al. Diagnostic and treatment peculiarities of iatrogenic lesions of major arteries and veins. *Angiologia I sosudistaya khirurgia*, 1997, 3 (Appendix), p. 197. (in Russian)
4. *Handbook on diagnostics and differential diagnostics of surgical diseases*. V.G. Astapenko, ed. Minsk, Belarus publishers, 1998, 432 p. (in Russian)
5. Tutov E.G., Semenov A.P. *Aneurysms of peripheral arteries – diagnostics and tactics of surgical treatment. Progress and problems in treatment of cardiac and vascular diseases*. SPb, 1997, 147. (in Russian)



# Ultrasound Signs of Portal Vein Thrombosis. Asymptomatic Disease Course (Clinical Case)

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Portal vein thrombosis (PV) is a process of thrombus formation until the complete occlusion of the vessel lumen draining the gastrointestinal organs. Portal vein thrombosis is a rare disease of hepatic vessels. It can result from a large number of different diseases and remain asymptomatic or can manifest as symptoms of the underlying disease. Disease diagnostics is complicated. In portal vein thrombosis, prognosis is always serious and unfavorable, lethal outcomes are often observed as a result of bleedings or hepatic coma.

Main trunk thrombosis of the portal vein in Russia was for the first time intravitaly diagnosed by S.P. Botkin in 1862. In 1934, N.D. Strazhesko was the first to describe intravitaly recognized thrombosis of the right branch of the portal vein trunk in the world literature, and he developed symptomatology for the right branch obstruction of the portal vein based on his own studies and literature data.

There are no reliable data on the incidence of portal vein thrombosis. According to post-mortem findings, thrombosis is registered in 0.14–0.34% of all autopsies (L. Lissauer, 1908; L.T. Webster, 1921; E.C. Pallette, 1936). According to other data (A.I. Gritsyuk, 1973), during the autopsy of subjects who died from major cardiovascular diseases (atherosclerosis, hypertensive disease, endocarditis and heart defects) portal vein thrombosis was observed in 0.56% of cases (in 10 out of 1763 died subjects), which accounts for 0.8% of all thromboembolisms developing during these diseases. It is known that portal vein thrombosis is registered in up to 30% of patients with hepato-

cellular carcinoma and in up to 5% of patients with portal hypertension associated with liver cirrhosis.

Development of this disease, as well as other venous thromboses, may be explained by Virchow's triad including the following elements.

1. Injury of the venous wall during the surgery.

2. Decreased blood flow velocity in the portal vein: compression of the vessel from the outside by the tumor, scarrings, echinococcal cyst, by alveococcus; chronic heart failure; constrictive pericarditis; Budd–Chiari syndrome (thrombosis of hepatic veins).

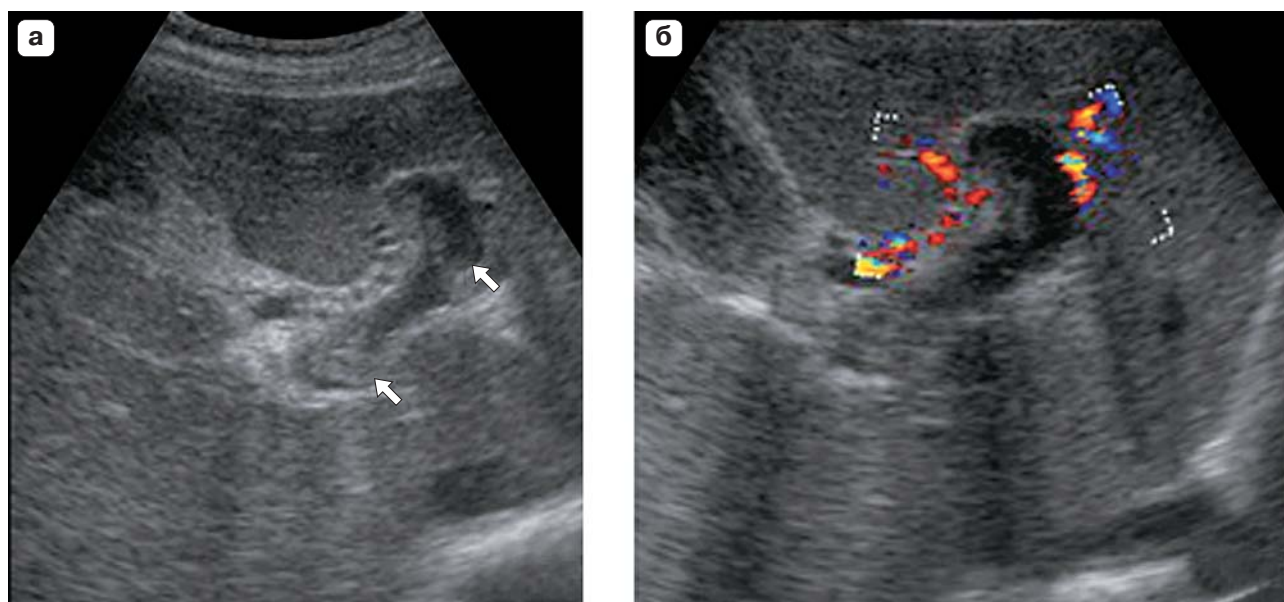
3. Increased blood coagulation or changes in the cell elements ratio: during the post-operative period, especially in oncologic patients, and also after splenectomy; during inflammatory processes as complication of acute appendicitis, in purulent cholangitis and lymphadenitis of hepatoduodenal ligament, ulcerative colitis; pancreonecrosis; umbilical infection during the neonatal period (neonatal septicemia, omphalitis, contamination during catheterization of umbilical vein for replacement blood transfusion); during pregnancy complications (in particular, during eclampsia); in some hematologic diseases causing increased blood clotting (e.g. Banti's pseudosyndrome in visceral leishmaniasis).

Clinical picture depends on localization and extent of portal vein thrombosis, the rate of its development and the nature of predisposing liver disease. The most severe manifestation of the disease is hepatic infarction or atrophy of its segment. However, in 1/3 of cases thrombosis forms slowly which results in development of collaterals, the portal vein eventually recanalizes, and its cavernous transformation is observed. Nevertheless, portal hypertension develops even in relatively favorable disease course.

When diagnosing portal vein thrombosis, attention should be paid to coagulogram which demonstrates the following: increased level of fibrinogen, appearance of activated fibrino-

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**Fig. 1.** Echogram of portal vein thrombosis. a – B-regimen. Non-homogenous mass of increased echogenicity with uneven ill-defined contours in the portal vein lumen (arrows); b – color flow mapping (CFM) regimen. Complete absence of Doppler signals inside the vessel lumen; Doppler signal is detected in small collaterals.

gen B, increased prothrombin ratio (PR), reduced blood clotting time.

During ultrasound examination (US) in seroscale regimen, non-homogenous mass of increased or mixed echogenicity with uneven ill-defined contours which obturates the blood flow may be observed; its dimensions may vary from 0.5 cm till complete occlusion of portal vein and/or its branches (Figure 1, a). Echogenicity of the thrombus is more increased when compared with the blood surrounding it. However, at early stages of development, echogenicity may differ so slightly that it is extremely difficult to visualize the thrombus. Increased vessel diameter with ill-defined contours, enlarged liver with decreased echogenicity, enlarged spleen may be observed. Prime causes of portal vein thrombosis may be determined: hepatocellular carcinoma, metastases, liver cirrhosis, pancreatic neoplasms etc. Liver abscesses may be detected in pylephlebitis.

In CFM, complete or partial absence of Doppler signals inside the vessel lumen is observed; in case of partial thrombosis, the signal is registered parietally around the thrombus partially occluding the vein or in the narrow collaterals (Figure 1, b). In case of partial thrombosis, a Doppler signal with signs of turbulence is observed together with increased blood flow velocity. In tumor thrombosis, blood flow may be pulsating or uninterrupted. Small and large collaterals are visualized. In case of cavernous transformation of the portal vein, flattened Doppler curve with mean blood flow velocity

less than 8 cm/sec is registered in CFM regimen in the collaterals. Cavernous venous malformations, spontaneous porto-portal, porta-caval and splenorenal shunts are possible.

During computed tomography (CT), the thrombus is detected as a filling defect in the portal vein lumen which does not enhance the signal.

In magnetic resonance imaging (MRI), the areas of pathological signal with the same intensity as surrounding tissues are detected on T1-weighted images and with increased intensity on T2-weighted images.

Angiography is a method of final diagnosis confirmation. Due to safety concerns, venous phase of superior mesenteric angiography is used more often, splenic portography is conducted less often. Either the filling defect is observed in the portal vein, or it is not contrasted at all.

Depending on thrombus localization, there are three types of portal vein thrombosis: radicular type (thrombosis of the splenic vein and of mesenteric vessels); terminal type (thromboses of small branches and capillaries of the portal vein in the liver); trunk thrombosis (in the portal vein trunk) (1–3).

Moreover, portal vein thrombosis can be acute (after splenectomy, in cirrhosis) and chronic (it develops for a long time ranging from few months till few years) (1–3).

Stages of thrombosis.

1. Acute – echogenic thrombus. Portal vein may be enlarged.

2. Subacute – thrombus and small collaterals are visualized. Portal vein may be enlarged.

3. Chronic – large collaterals in the projection of obliterated portal vein (cavernous transformation of the portal vein). Portal vein is diminished or cannot be visualized (1–3).

## Treatment

Below mentioned therapy is used only for genuine portal vein thrombosis. In all other cases it is necessary to determine a direct cause of this complication.

### Medication therapy

**Anticoagulants** Emergency care: heparin 40,000–60,000 U by intravenous (i/v) drip infusion for 4–6 hours, then 40,000 U/day (from Day 1 to Day 8–10) intramuscularly (i/m). The dose of the drug should be based on blood clotting time, plasma tolerance to heparin and results of thromboelastography. Maintenance therapy: 1–3 days prior the completion of heparin administration, indirect anticoagulants (phenindione, ethyl biscoumacetate, acenocoumarol) are prescribed, the dose is chosen individually (decrease of PR till 40%). For example, the doses of phenindione are as follows: on Day 1 – 0.12–0.18 g/day (divided into 3–4 doses), on Day 2 – 0.09–0.06 g/day, on subsequent days – 0.03–0.06 g/day (depending on PR). Contraindications for prescribing anticoagulants. Absolute contraindications: severe bleeding, recent (within 1 month) neurosurgeries, pregnancy, intolerability reactions. Relative contraindications: recent severe bleedings, surgeries (except for neurosurgeries), a history of ulcer disease or recent stroke (not related to embolism).

Thrombolytic drugs, e.g. fibrinolysin (20,000–40,000 U adding 10,000 U of heparin to each 20,000 U of fibrinolysin) i/v over 3–4 hours, streptokinase, streptodectase.

Rheopolyglukin, rheogluman (400–800 mL/day i/v for 3–5 days).

In pylephlebitis – broad spectrum antibiotics, e.g. imipenem+cilastatin up to 4 g/day i/v divided into 3–4 doses.

### Surgical treatment

**Conservative methods.** The usage of Sengstaken-Blakemore tube. After introducing the tube into the stomach, the air is inflated in the cuffs, compressing veins of cardia and the lower third of esophagus. In order to avoid decubitus ulceration, balloons are deflated every 5–6 hours for 5–10 minutes. A total dura-

tion of the tube usage should not exceed 48 hours.

**Injection sclerotherapy:** during esophagoscopy, sclerosing agent decilatum (trombovar) is introduced into esophageal varices, causing their thrombosis.

- Surgical treatment is used if conservative treatment is unsuccessful

- If the splenic vein is patent, the surgery of choice is to create splenorenal anastomosis

- Otherwise, mesenteric-caval anastomosis is created using a vascular prosthesis of large diameter (16–18 mm) between the superior mesenteric vein and inferior vena cava

- In case of continuous esophageal bleeding, stitching of esophageal varices may be performed, e.g. Tanner operation (transverse transection of the stomach in the cardia with subsequent end-to-end suturing of its walls)

- In pylephlebitis – lancing and draining of abscesses in the liver.

We would like to bring a clinical case from our practice to your attention.

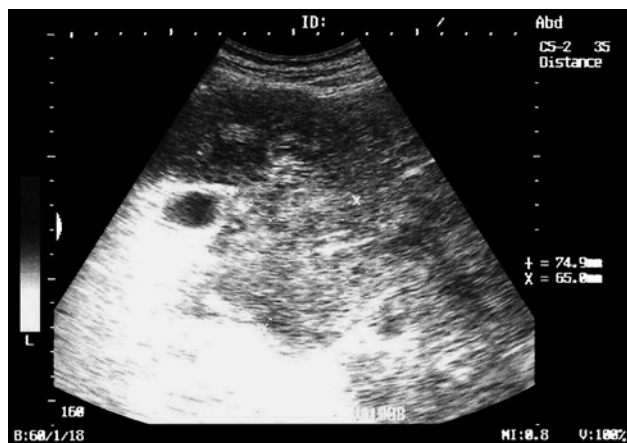
**Patient K., 61 years old.** Since 2007, the patient was repeatedly observed and treated in the Moscow City Center of Interventional Cardiology for coronary heart disease and atherosclerosis of lower limb arteries.

**Medical history.** In 2007, he had non-Q-wave posterior diaphragmatic myocardial infarction, involving the lateral wall. At the pre-hospital stage, systemic thrombolysis with actilyse was performed to the patient. During coronary angiography, 80% critical stenosis of the middle third of the left anterior descending artery (LAD), occlusion of the proximal third of the left circumflex coronary artery (LCX), and 70% stenosis of the middle third of the right coronary artery (RCA) were detected. Transluminal angioplasty and stenting of the LCX using Bx Sonic stent 3 × 18 mm were conducted. **Concomitant disease:** atherosclerosis of lower limb vessels for which stenting of right common hepatic artery (CHA) was performed with good effect. In June (14.06.11), he was hospitalized in the clinic for elective endovascular procedures on the LAD and RCA, as angina attacks persisted. The patient was taking the following medications: zilt, cardiomagnyl, concor, co-renitec.

On general examination, an attending physician paid attention to increased liver; due to this fact ultrasound examination of hepatobiliary organs was scheduled. According to the patient, he experienced pain in epigastrium, abdominal distension and constipation for the past two-three weeks.

The following was detected at *ultrasound examination* (Fig. 2–5): increased dimensions of right and





**Fig. 2.** Echogram of the right liver lobe. (Sequence of areas with increased and decreased echogenicity of hepatic parenchyma – areas of parenchymal necrosis).



**Fig. 3.** Echogram of the right liver lobe – areas of parenchymal necrosis.



**Fig. 4.** Echogram of the main trunk of the portal vein and its right branch.



**Fig. 5.** Echogram of the main trunk of the portal vein (dilated to 19.0 mm).

left liver lobes (oblique vertical dimension of liver was increased up to 20.0 cm), mixed echogenicity of parenchyma with areas of increased and decreased echogenicity. Also dilation of the portal vein up to 18.0 mm was noticed. Isoechogenic inclusion was visualized in the venous lumen which did not completely obstruct the venous lumen. Partial coloring of the venous lumen was recorded at color Doppler examination, almost no collapse was observed depending on the respiration phase.

The patient was recommended to undergo computed tomography.

**CT data.** Liver is enlarged, with diffusely non-homogenous structure, with multiple areas of significant differences in parenchymal density. Massive thrombosis is detected in the lumen of the portal vein with signs of luminal subocclusion spreading on the main branch of the right lobe, and multiple thrombosis of a smaller lobe. Other abdominal and retroperitoneal organs are without pathological changes.

Laboratory data are without significant changes, except for increased level of total bilirubin up to

20.8 mmol/L, increased gamma-glutamyltransferase up to 249 U/L, increased level of C-reactive protein up to 14.4 mg/L.

#### HEMOSTASIS TESTING dated 15.06.11.

		Normal value
Platelet count, $10^9$ /L	186	150–390
Aggregation time, seconds	36	52–66
% of aggregation	30	47–67
% of desaggregation	75	0–6
Prothrombin ratio	1.03	0.88–1.13
International normalized ratio (INR)	1.03	0.85–1.15
Fibrinogen, g/L	2.7	2–4
Activated partial thromboplastin time (APTT), seconds	35.7	24–34

The patient was consulted by a general surgeon at N.V. Sklifosovsky Research Institute of Emergency Medicine, where he was transferred to for the further treatment.



At N.V. Sklifosovsky Research Institute of Emergency Medicine the patient was examined and was diagnosed with hepatocellular cancer complicated by portal vein thrombosis and Grade 1 esophageal varices. After discharge, the patient was referred to the oncologic center for consult and observation.

In two months the patient's condition dramatically worsened, due to this he was hospitalized in the City Clinical Hospital No. 62 with suspected acute gastrointestinal bleeding in a terminal stage. Despite performed resuscitation procedures, the patient died on the next day (August 7, 2011).

Therefore, taking into consideration the above mentioned clinical case, it may be concluded that portal vein thrombosis is a serious pathological condition which may develop as an independent disease, and may be a complication of a more serious process. Portal vein thrombosis may result in lethal outcome despite the absence of marked clinical presentation. This case is an example of asymptomatic

course of the main severe disease (hepatic cancer) resulting in portal thrombosis, which, in turn, was an incidental finding during the ultrasound abdominal examination.

## References

1. Zhestovskaya S.I., Grakova L.S., Aksenova N.A. Clinical use of duplex scanning for detecting collateral blood flow in portal hypertension. *Pervaya kraevaya*, 2001, 10, 10–12. (in Russian)
2. Kuntsevich G.I. Ultrasound diagnostics in abdominal and vascular surgery. Minsk, Kavalier Publishers, 1999, 252 p. (in Russian)
3. Mit'kov V.V. Dopplerography in diagnostics of liver, gallbladder, pancreas diseases and diseases of their vessels. M., VIDAR, 2000, 152 p. (in Russian)
4. Scoutt L.M., Zavin M.L., Taylor K.J. Doppler ultrasound clinical application. *Radiology*, 1990, 174, 309–319. (in Russian)
5. Lelyuk V.G., Lelyuk S.E. Ultrasound angiology. M., Real'noe vremya, 2003, 332 p. (in Russian)
6. Sinel'nikov R.D., Sinel'nikov L.R. Atlas of human anatomy. M., Meditsina, 1996. (in Russian)

# Transcatheter Aortic Valve Implantation and Endovascular Procedures on Coronary Arteries. What is Primary? (Review of Literature)

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Increase in life expectancy resulted in more frequent aortic valve replacements in patients aged older 80 years; however, mortality rate after conventional valve replacement in patients of this age group is rather high (Yamashita et al., 2012). Nevertheless, in patients at high surgical risk and in inoperable patients transcatheter aortic valve implantation (TAVI) more frequently replaces conventional surgery (Dworakowski and Maccarthy, 2012).

However, the question regarding which surgery to prefer is not finally solved, especially if such patients have a history of coronary artery bypass grafting. According to Yegaden et al. (2012), 1 year after surgery survival rate was 100% in surgical group and in TAVI group when using transfemoral approach. Mortality rate was 73% in TAVI group with transapical approach.

Coronary heart disease (CHD) is registered in more than 50% of patients older than 70 years with severe aortic valve stenosis who underwent transcatheter aortic valve implantation (Dewey et al., 2010). Combination of surgical aortic valve replacement and coronary artery bypass grafting is a gold standard for treatment of patients with aortic valve stenosis and concomitant coronary heart disease, although it is associated with higher surgical risk (Dimorakis et al., 2011). Moreover, a significant proportion of such patients are not suitable for surgery due to contraindications. CHD increases the intra-operative risk during TAVI and concerns regarding the approach to the coronary artery after valve replacement support conduction of percutaneous coronary interventions prior to TAVI (Gautier et al., 2011). While myocardial revas-

cularization affects the surgical outcome in patients who underwent surgical aortic valve replacement, the influence of percutaneous coronary interventions (PCIs) in patients who underwent transcatheter aortic valve implantation has not yet been determined (Jatte et al., 2012, Wenaweser et al., 2011).

The studies are currently aimed at solving the problem of safety and possibility of conducting PCI in patients with significant lesion of coronary vessels who are scheduled for TAVI. According to the opinion of Pasic et al. (2012), the treatment strategy (when and where) for coronary heart disease in patients selected for TAVI is not ultimately determined. The authors performed endovascular procedures on the coronary arteries prior to TAVI in 46 patients, and in 100% of cases they achieved angiographically good result. Mortality rate within 30 days was 4.3%. Survival rate in 36 months after the surgery was  $69.7 \pm 10.3\%$ . According to the authors data, a single-stage surgery is safe and effective.

Abdel-Wahab et al. (2012) consider that TAVI is a prospectively new method of treatment of patients with severe aortic valve stenosis at high surgical risk. Fifty five out of such 125 patients underwent PCI at least 3 months prior to supposed TAVI (mean interval was 10 days) or as single-stage procedure, and the rest 70 patients underwent isolated TAVI. All patients were implanted CoreValve prosthesis (Medtronic). Thirty-day mortality rate was 2% (TAVI + PCI) and 6% (isolated TAVI) ( $p = 0.27$ ). There were no significant differences in complications. Therefore, preliminary endovascular treatment of coronary heart disease prior to valve replacement may be possible and useful in this situation.

Conradi et al. (2011) consider combination of percutaneous aortic valve implantation and percutaneous coronary intervention as an alternative strategy in high-risk patients. Twenty eight patients who underwent TAVI and PCI and who were denied surgical treatment were examined. The first group where PCI was per-

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formed prior to the scheduled TAVI (mean interval was 14 days) included 21 patients. The second group consisted of 7 subjects who underwent PCI directly before TAVI. Neither acute myocardial infarction (AMI) nor cerebrovascular accident (CVA) was observed in patients. Thirty-day mortality rate was 7.1%. This strategy of staged or single-stage TAVI and PCI turned out to be possible and safe in high-risk patients.

The discussion on the following topic was published in *The heart org* in 2011 under the number 12229197: "The TAVI patient with CAD: Experts debate whether and when to do PCI." The experts opinions have divided. According to Nadra (2011), conduction of percutaneous coronary interventions prior to TAVI has an advantage of providing the easiest approach to the coronary arteries and reducing the risk of myocardial ischemia during valve implantation which, in turn, may reduce the risk of left ventricular dysfunction and ventricular arrhythmias. On the other hand, Doctor Tolg (2011) considers that the patients scheduled for TAVI start taking double desaggregant therapy before the intervention, and PCI itself will be a high risk procedure regarding aortic stenosis. Meanwhile, percutaneous coronary interventions after valve implantation reduce the risk associated with endovascular procedures in patients with aortic stenosis; however, the approach to the coronary arteries is more complicated. Redwood (2011) noted that TAVI is already a high-risk procedure for a patient, and there is a serious risk of stent thrombosis in such patient after recent revascularization associated with the surgery conducted at the background of long-term intake of double anti-aggregant therapy. Hayashida et al (2012) demonstrated that one-year survival after TAVI in females is significantly higher than in males (76% vs 65%).

In October 2011, ACTIVATION study devoted to percutaneous coronary intervention prior to transcatheter aortic valve implantation commenced; it included 310 patients from 20–30 Great Britain and European hospitals.

The patients were randomized into 2 groups: isolated TAVI and TAVI in combination with primary percutaneous coronary intervention. Mortality and repeated hospitalization within a year will be the primary endpoints. The study is planned to be completed by October 2015.

In March 2012, the study of Gasparetto et al. (2012) and Ussia et al. (2012) was published which demonstrated that coronary revasculari-

zation before TAVI is safe and has the same results as isolated TAVI.

Thus, transcatheter aortic valve implantation has recently become a method of choice in treatment of aortic valve stenosis, especially in patients at high surgical risk. Currently, there is no developed strategy regarding how and when to treat CHD in patients referred for TAVI. At the same time, simultaneous single-stage treatment of both pathologies is considered as one of the possible solutions.

## References

1. Yamashita M.N., Ye J., Jamieson W.R. Conventional aortic valve replacement remains a safe option in patients aged >70 years: a 20-year experience. *J. Heart Valve Dis.*, 2012, 21 (2), 148–155.
2. Dworakowski R., Maccarthy P. Where should transcatheter aortic valve implantation go beyond 2012; *J. Cardiovasc. Med.* 2012, May 24.
3. Yegaden O., Lapeze J., Farhat F., de Gevigney G. Aortic valve stenosis after previous coronary bypass: Transcatheter valve implantation or aortic valve replacement? *J. Cardiothorac. Surgery*, 2012, 7 (1), 47.
4. Dewey T.M., Brown D.L., Herbert M.A. et al. Effect of concomitant coronary artery disease on procedural and late outcomes of transcatheter aortic valve implantation. *Ann Thorac. Surg.*, 2010, 89 (3), 758–767.
5. Dimarakis I., Rehman S.M., Grant S.W. et al. Conventional aortic valve replacement for high-risk aortic stenosis patient not suitable for transcatheter aortic valve implantation: feasibility and outcomes. *Eur. J. Cardiothorac. Surg.* 2011, 40 (3), 743–748.
6. Jaffe R., Finkelstein A., Lewis B.S. et al. Stenting of the unprotected left main coronary artery in patients with severe aortic stenosis prior to percutaneous valve interventions. *Cardiovasc. Revasc. Med.*, 2012, 13 (2), 90–94.
7. Pasic M., Dreysee S., Unbehaun A. et al. Combined elective percutaneous coronary intervention and transapical transcatheter aortic valve implantation. *Interact. Cardiovasc. Thorac. Surg.* 2012, 14 (4), 463–468.
8. Abdel-Wahab M., Mostafa A.E., Geist V. et al. Comparison of outcomes in patients having isolated transcatheter aortic valve implantation versus combined with preprocedural percutaneous coronary intervention. *Am. J. Cardiol.*, 2012, 109 (4), 581–586.
9. Conradi L., Seiffert M., Franzen O. et al. First experience with transcatheter aortic valve implantation and concomitant percutaneous coronary intervention. *Clin. Res. Cardiol.*, 2011, 100 (4), 311–316.
10. The TAVI patient with CAD: Experts debate whether and when to do PCI. *The Heart org.*, 2011, № 1229197
11. Hayashida K., Morice M.C., Chevallier B. et al. Sex-related differences in clinical presentation and outcome of TAVI for severe aortic stenosis. *J. Am. Coll. Cardiol.*, 2012, 59, 566–571.
12. Gasparetto V., Fracaro C., Tarantini G. et al. Safety and effectiveness of a selective strategy for coronary artery revascularization before transcatheter aortic valve implantation. *Catheter Cardiovasc. Interv.* 2012, Mar 28.

13. Ussia G., Barbanti M., Colombo A. et al. Impact of coronary artery disease in elderly patients undergoing transcatheter aortic valve implantation. *Int. J. Card.*, 2012, Mar 27.
14. Gautier M., Pepin M., Himbert D. et al. Impact of coronary artery disease on indication for transcatheter aortic valve implantation and on procedural outcomes. *Eurointervention*. 2011, 7 (5), 549–555.
15. ACTIVATION: Percutaneous coronary intervention prior to transcatheter aortic valve implantation: a randomized controlled trial, 2011; ISRCTN 75836930.
16. Wenaweser P., Pilgrim T., Guerios E. et al. Impact of coronary artery disease and percutaneous coronary intervention on outcomes in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation. *Eurointervention*., 2011, 7 (5), 541–548.



# Percutaneous Coronary Interventions using Drug-Eluting Stents: Past, Present and Future (Review of Literature)

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Cardiovascular pathology is one of the most common causes of disability and mortality among the adult population in the industrially developed countries, including the Russian Federation (1, 2). According to the recent data from the World Health Organization, cardiovascular diseases annually are the cause of more than 30% of all lethal outcomes worldwide, and 32 million of people have a history of myocardial infarction (MI) (3). In a general structure of mortality, the proportion of cardiovascular diseases in the Russian Federation is the highest among the world's developed countries and reached 55% by 2000; coronary heart disease (CHD) accounts for more than 36% (4).

Invasive percutaneous methods of treatment of coronary atherosclerosis were for the first time used by Andreas Gruntzig at the end of 1970s, when he and Senning described the procedure called percutaneous transluminal coronary angioplasty. They reported that 6 out of 32 patients (19%) who underwent balloon angioplasty experienced restenosis or repeated narrowing of the vessel a few months after the initial procedure (5). Subsequent studies in a large number of patients after coronary angioplasty reported about 33% restenosis rate (6).

## Restenosis phenomenon after percutaneous interventions

For the first time, intravascular endoprosthesis (stent) for support of the vessel wall after transluminal angioplasty was implanted in the coronary artery by U. Sigwart in 1986 in Switzerland. It was a nitinol self-expanding Wallstent (7). Endografting provided a high direct success

rate and eliminated a number of serious complications typical for transluminal angioplasty such as pronounced dissections and acute occlusions of the coronary arteries (CA) (8).

It was found that stents significantly reduced the rate of restenosis – a repeated lumen narrowing in the vessel on which angioplasty had been previously performed (9). Although enhancement of technologies, development of new prostheses, alloys, as well as drug modification of the stents significantly reduced the rate of restenosis, but they did not solve this problem.

Histopathology of restenosis after percutaneous coronary interventions (PCI) varies and is generally characterized by neointimal tissue proliferation. Degree of neointimal proliferation directly depends on the severity of endothelial lesion at PCI, on the intensity of inflammatory response, and on biocompatibility of the implant itself in case of implantation of the coronary stent. Clinical parameters may positively or negatively affect the rate of restenosis development. Conducted large multicenter studies have demonstrated the efficacy of using drug-eluting stents; however, there are a lot of questions regarding the mechanism of restenosis which have not been answered yet.

Restenosis has many clinical definitions. The term “angiographic restenosis” is usually based on more than 50% difference in the diameter of stenosis at the stented site and native vessel. However, while angiographic parameters of restenosis complement the understanding of restenosis mechanisms, clinical results should be considered as genuine criterion of treatment success (10). Clinical definition of success includes repeated interventions which are usually based on the clinical symptoms or other signs of myocardial ischemia.

## Predictors of restenosis

Goldberg et al. (11) assessed 456 CA lesions with restenosis in the stent. They defined diffuse restenosis as restenosis more than 10 mm long,

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or as an expansion of the initial lesion, or as a restenotic narrowing more pronounced than the initial one. The authors determined that diffuse restenosis was associated with the smaller reference diameter of an artery, greater lesion extent, female gender, longer stent and with the use of spiral stents. Other studies demonstrated relationship between restenosis and multiple stenting, smaller final minimal lumen diameter (12) and insufficient use of intravascular ultrasound (IVUS) due to technical and financial difficulties (13).

Many large studies showed that patients with diabetes mellitus (DM) had the higher rate of restenosis after stent implantation as compared with patients without diabetes (14). Another study demonstrated that not only restenosis contributes to the higher rate of revascularization in diabetes, but progression of coronary atherosclerotic lesion as well (15). Based on the large number of conducted studies, it may be concluded that diabetes really predisposes to restenosis in the stent; however, the intensity of diabetes impact on restenosis remains controversial.

### **Drug-eluting stents: evolution or revolution?**

To date, most of the used coronary stents consist of medical grade 316L stainless steel, alloys of cobalt and chrome or nitinol (alloy of nickel and titanium), from 8 to 38 mm long and from 2.25 to 5 mm in diameter (16).

Detailed understanding of restenosis process in the stent has led to investigating a wide range of drugs aimed at various pathways leading to restenosis. The first two drug-eluting stents (DES), which appeared in Europe, USA and Canada in 2003–2004, were coated with sirolimus and paclitaxel (17). Sirolimus and paclitaxel are both immunosuppressive and antiproliferative agents, but their mechanism of action varies.

Release of the drug should be predictable. Transporting binding delivery agent (most often, a polymeric carrier) should be biologically inert and should follow the changes in the stent configuration during expansion and implantation.

Polymeric coating, as well as its type, also influence the rate of restenosis and thrombosis (18), as it may be associated with vascular inflammation and more prolonged healing (19). Biologically compatible coatings of natural phospholipid polymer are currently in the clinical use (20).

### **Clinical studies of drug-eluting stents**

To date, a large number of multicenter randomized studies of drug-eluting stents have been conducted, proving their efficacy regarding restenosis as compared with bare metal stents (BMS). All studies have been repeatedly covered earlier. However, thorough meta-analysis of the largest number of such studies is what has scientific and practical importance.

Sondhi et al. (21) in 2006 performed meta-analysis of 12 studies devoted to this problem, which were conducted from 1996 to 2005 (4902 patients). According to the conclusions of the group of investigators, DESs do not affect the total risk of death or combined risk of death or MI as compared with BMSs. DESs, nevertheless, are associated with a low basic risk of restenosis as compared with BMSs (8% for DESs and 31% for BMSs). DESs required target lesion revascularization (TLR) in 4% as compared with BMS, for which TLR was 15%.

Kastrati et al. (22) conducted meta-analysis of 14 studies comparing DESs and BMSs (4958 patients). The investigators confirmed that the use of sirolimus-eluting stents does not cause a significant positive effect on the overall long-term survival and major adverse clinical events (MACE) as compared with BMS. Total risk of death and combined risk of death or MI were almost identical both for the patients with implanted DESs, and for the patients with BMSs. The authors reported significant reduction in the rate of repeat revascularizations (TLR) related to the use of sirolimus-eluting stents and almost no significant difference in the overall risk of thrombosis for DES and BMS. Nevertheless, a slight increase in the risk of sirolimus-eluting stent thrombosis was confirmed after the first year.

In Camenzind (23) meta-analysis, clinically oriented meta-analysis was focused on the cases of death, Q-wave MI and cumulative number of death and Q-wave MI cases, as they better reflect the rate of stent thromboses, the use of limiting thrombosis definitions (as, for example, late stent thrombosis according to angiography data). According to the most recent result, overall mortality and Q-wave MI cases were by 38% (sirolimus) and by 16% (paclitaxel) higher when using DESs as compared with control, where BMSs were used.

In total, the studies comparing sirolimus- or paclitaxel-coated stents were too small to make final conclusions regarding the advantage of two types of antiproliferative coatings. Meta-

analysis revealed that restenosis occurred less often in sirolimus group (9.3%) as compared with paclitaxel group (13.1%). As for the rate of stent thrombosis, mortality, including mortality due to MI, was similar in both groups of patients. Regardless of the fact that this meta-analysis supports sirolimus regarding restenosis, more large-scale studies with additional statistical processing are required in order to obtain more reliable results (24).

### **Indications for using various types of coronary stents**

Appearance of drug-eluting stents as well as improvement of technologies and techniques discovered new opportunities in treatment of complex and unusual CA lesions. The length of lesion as well as diameter of the vessel were independent predictors of restenosis by themselves. Meta-analysis demonstrated that stenting of small-diameter vessels significantly decreased the rate of repeat revascularizations as compared with balloon angioplasty, which was previously widely used for the treatment of small caliber lesions (25). Recent TAXUS-VI studies demonstrate that drug-eluting stents decrease the degree of restenosis in small caliber vessels (26).

Different studies comparing stenting with transluminal angioplasty of CA occlusions reported that stenting reduces the degree of angiographic and clinical restenosis and re-occlusion (27). Recently, a number of studies comparing drug-eluting stents with their metal analogies confirmed the high efficacy of the former (28).

For treatment of bifurcation lesions, different methods of stenting are used, each of which has its own advantages and indications. The use of coated stents is accompanied by a lower rate of restenoses; however the degree of restenosis remains higher in the side branches as compared with the main vessel (29).

Efficacy and safety studies demonstrated that stenting of unprotected stenosis in the trunk may be a real alternative to coronary artery bypass grafting (30). Analysis of recent studies showed a leading role of coated stents in treatment of trunk lesions. SYNTAX study also demonstrated good results of interventions using coated stents as compared with coronary artery bypass grafting (31).

### **Thrombosis as an Achilles' heel of drug-eluting stents**

The use of stents has its disadvantage (namely, thrombosis). There are two different

types of thromboses: early stent thrombosis which is observed within the first 30 days, and late stent thrombosis observed after 30 days. Orford et al. (32) studied 4500 patients of Mayo clinic and reported 0.51% rate of thrombosis. The problem is that the patients with stent thrombosis have a 70–87% risk of lethal outcome or MI.

Late stent thrombosis may be observed with decreased re-endothelialization of the vessel and implanted stent. According to Ong et al. data (33), angiographic rate of late thromboses is approximately 0.35%; however, the clinical rate is probably higher, because some cases such as sudden cardiac death or acute myocardial infarction (AMI) may not be registered. The cause of late thromboses is unknown and is currently being studied. The study is carried out in three directions: poor re-endothelialization due to the toxic nature of the medicinal product, allergy to the medicinal product and remodeling of the vascular lumen (19).

Continuous neointimal formation for a long time is a phenomenon observed with drug-eluting stents. Unlike metal stents, in which the peak of neointimal formation is at 6 months and then it regresses, actual duration of this process in drug-eluting stents which delay neointimal growth is unknown.

### **Prospects of development of CHD endovascular treatment**

Thus, the existing stents are apparently an intermediate link in technical development of invasive transcatheter technique for coronary atherosclerosis treatment. Conducted multiple and large-scale studies revealed a large number of disadvantages for widely used implanted frame devices.

A tendency for the further development of endovascular treatment of cardiovascular pathology has many sides. To date, third-generation drug-eluting stent with biodegradable polymer on the lactic acid basis (PLA) has been developed and is successfully used. In the future, a stent with such system of local drug delivery is able to draw closer an efficiency of drug-eluting stents and safety of bare-metal stents. The first of such mass-production stents was Nobori stent (by Terrumo). R. Virmani et al. demonstrated complete endothelialization on Day 28 after the stent implantation in an experiment. The stent is characterized by its unilateral abluminal biodegradable polymer coating with a cytostatic agent (sirolimus A9), that provides timely endothelialization of the stented

segment. At that, manageable polymer washing-out decreases the proliferative response during the acute period of restenosis formation, eventually the stent becomes a bare-metal stent. Conducted randomized studies Nobori 1, 2, PK, Core with 9-month long-term period demonstrated efficacy and safety of such stents; however, the impact on long-term survival and on the incidence of severe cardiac complications was not assessed (34).

A wide usage of stents has demonstrated that their permanent presence in the vessel causes thrombosis, chronic inflammation and neointimal proliferation, leading to restenosis. Permanent vascular stent impairs the vessel geometry, and the polymer used as a vehicle for local drug delivery may induce vessel irritation, endothelial dysfunction, hyperreactivity of the vessel and chronic inflammation at the site of implantation (35). Implantation of metal constructions in the CA may further not only complicate the conduction of necessary surgical interventions, but creates artifacts for modern non-invasive methods of cardiac imaging.

In contrast to bare metal stents, bioabsorbable stents, after being completely eliminated from the vessel, leave behind only an expanded vascular lumen, allowing restoration of vasoreactivity with potential vascular remodeling. Late stent thrombosis is also unlikely in a situation when the stent is gone from the vascular lumen, which does not require prolonged antithrombotic therapy. Bioabsorbable stents may deliver drugs or genes, and perhaps play a role in treatment of unstable plaques (36). Such stents were developed and were tested in pre-clinical and even clinical studies. Metal magnesium-based bioabsorbable stents have a potential comparable with stainless steel stents. Studies of their efficacy and safety in animals and humans are based exactly on this feature. Heublein et al. (37) conducted a series of pre-clinical studies with magnesium stents which demonstrated a high level of complete stent degradation within 60–90 days since the moment of implantation and good biocompatibility. When comparing magnesium alloy stent with a 316 L stainless steel stent in animals, positive vessel remodeling was observed in a magnesium stent with a reduction of neointimal growth and complete absorption of the stent within an interval from 30 to 56 days.

Currently, there are ongoing research projects, which combine magnesium stents with local delivery of the drugs preventing restenosis. It turned out to be necessary, as relatively

fast (30–60 days) disappearance of the stent from the vessel triggers subsequent inflammatory reaction and neointimal proliferation (38). Therefore, if the stents coated with antiproliferative agents slow or stop inflammation and neointimal growth, then optimal results may be achieved in coronary revascularization with magnesium used as a platform (39).

## References

1. Sehgal S.N., Baker H., Vezina C. Rapamycin (AY-22, 989) a new antifungal antibiotic. Fermentation, isolation and characterization. *J. Antibiot. (Tokyo)*, 1975, 28, 727–735.
2. National Heart, Lung, and Blood Institute (NHLBI). NHLBI fact book fiscal year 1997. Bethesda, MD: NHLBI, 1998.
3. Bokeria L.A., Gudkova R.G. Cardiovascular surgery-2000. Moscow, Scientific Center of Cardiovascular Surgery named after A.N. Bakulev, Russian Academy of Medical Sciences, 2001, 3–5.
4. Belenkov Yu.N., Mareev V.Yu., Ageev F.T. Epidemiological studies of cardiac failure: status of issue. *Serdechnaya nedostatochnost (Cardiac Failure)*, 2002, 2, 57–58.
5. Gruntzig A.R., Senning A., Siegenthaler W.E.. Nonoperative dilatation of coronary-artery stenosis: percutaneous transluminal coronary angioplasty. *N. Engl. J. Med.*, 1979, 301, 61–68.
6. Holmes D.R. Jr., Vlietstra R.E., Smith H.C. et al. Restenosis after percutaneous transluminal coronary angioplasty (PTCA): a report from the PTCA Registry of the National Heart, Lung, and Blood Institute. *Am. J. Cardiol.*, 1984, 53, 77C–81C.
7. Myler R. Coronary and peripheral angioplasty: historical perspective. In: "Textbook of interventional cardiology", W.B. Saunders, 1999, 127–41.
8. Serruys P.W., Van Hout B., Bonnier H. et al. Effectiveness, costs and cost-effectiveness of a strategy of elective heparin-coated stenting compared with balloon angioplasty in selected patients with coronary artery disease: the BENESTENT II Study. *Lancet*, 1998, 352, 673–681.
9. Serruys P.W. ARTS I – the rapamycin eluting stent; ARTS II – the rosy prophecy. *Eur. Heart J.*, 2002, 23, 757–759.
10. Rosenschein U., Topol E.J. Uncoupling clinical outcomes and coronary angiography: a review and perspective of recent trials in coronary artery disease. *Am. Heart J.*, 1996, 132, 910–920.
11. Goldberg S.L., Loussarian A., De Gregorio J. et al. Predictors of diffuse and aggressive intra-stent restenosis. *J. Am. Coll. Cardiol.*, 2001, 37, 1019–1025.
12. Kasaoka S., Tobis J.M., Akiyama T. et al. Angiographic and intravascular ultrasound predictors of in-stent restenosis. *J. Am. Coll. Cardiol.*, 1998, 32, 1630–1635.
13. Lee S.G., Lee C.W., Jong M.K. et al. Predictors of diffuse-type in-stent restenosis after coronary stent implantation. *Catheter. Cardiovasc. Interv.*, 1999, 47, 406–409.
14. Mathew V., Gersh B.J., Williams B.A. et al. Outcomes in patients with diabetes mellitus undergoing percutaneous coronary intervention in the current era: a report from the prevention of REStenosis with tranilast and its outcomes (PRESTO) trial. *Circulation*, 2004, 109, 476–480.



15. Gilbert J., Raboud J., Gilbert J., Zinman B. Meta-analysis of the effect of diabetes on restenosis rates among patients receiving coronary angioplasty stenting. *Diabetes Care*, 2004, 27, 990–994.
16. Borovetz H.S., Burke J.F., Chang T.M. et al Application of materials in medicine, biology and artificial organs, in: Ratner B.D., Hoffman A.S., Schoen F.J., Lemons J.E. (Eds.). *Biomaterials Science*, 2nd edition, Elsevier Academic Press, Boston, 2004, 455: 4–79.
17. Baim D.S. New devices ifor percutaneous coronary intervention are rapidly making bypass surgery obsolete. *Curr. Opin. Cardiol.*, 2004, 19, 593–597.
18. Guagliumi G., Färb A., Musumeci G. et al Sirolimus-eluting stent implanted in human coronary artery for 16 months: pathological findings. *Circulation*, 2003, 107, 1340–1341.
19. Virmani R., Guagliumi G., Färb A. et al. Localized hypersensitivity and late coronary thrombosis secondary to a sirolimus-eluting stent: should we be cautious? *Circulation*, 2004, 109, 701–705.
20. Sousa J.E., Serruys P.W., Costa M.A. New frontiers in cardiology. Drug-eluting stents: part 1. *Circulation*, 2003, 107, 2274–2279.
21. James H.F. Rudd, John R. Davies, Peter L. Weissberg. *Atherosclerotic Biology and Epidemiology of Disease*. In: Topol E.J., ed. *Textbook of Cardiovascular Medicine*. New York: Lippincott Williams & Wilkins; 2007. Chapter 1.
22. Kastrati A., Mehilli J., Pache J. et al. Analysis of 14 Trials Comparing Sirolimus-Eluting Stents with Bare-Metal Stents. *N. Engl. J. Med.*, 2007, 356, 1030–1039.
23. Camenzind E. et al. ESC 2006. Abstracts.
24. Kastrati A., Dibra A., Eberle S. et al. Sirolimus-eluting stents vs paclitaxel-eluting stents in patients with coronary artery disease: meta-analysis of randomized trials. *JAMA*, 2005, 294 (7), 819–825.
25. Hausleiter J., Kastrati A., Mehilli J. et al. Predictive factors for early cardiac events and angiographic restenosis after coronary stent placement in small coronary arteries. *J. Am. Coll. Cardiol.*, 2002, 40, 882–889.
26. Ellis S., Popma J., Lasala J. et al. Relationship between angiographic late loss and target lesion revascularization after coronary stent implantation: analysis from the TAXUS-IV trial. *J. Am. Coll. Cardiol.*, 2005, 45 (8), 1193–2000.
27. Agostoni P., Valgimigli M., Biondi-Zoccai G.G. et al. Clinical effectiveness of bare-metal stenting compared with balloon angioplasty in total coronary, occlusions: insights from a systematic overview of randomized trials in light of the drug-eluting stent era. *Am. Heart. J.*, 2006, 151 (3), 682–689.
28. Hwang C.W., Levin A.D., Jonas M. et al. Thrombosis modulates arterial drug distribution for drug-eluting stents. *Circulation*, 2005, 111, 1619–1626.
29. Colombo A., Moses J.W., Morice M.C. et al. Randomized study to evaluate sirolimus-eluting stents implanted at coronary bifurcation lesions. *Circulation*, 2004, 109, 1244–1249.
30. Silvestri M., Barragan P., Sainsous J. et al. Unprotected left main coronary artery stenting: immediate and medium-term outcomes of 140 elective procedures. *J. Am. Coll. Cardiol.*, 2000, 35, 1543–1550.
31. Ong A.T., Serruys P.W., Mohr F.W. et al. The SYNergy between Percutaneous Coronary Intervention with TAXus and Cardiac Surgery (SYNTAX) Study: design, rationale and run-in phase. *Am. Heart. J.*, 2006, 151, 1194–1204.
32. Orford J.L., Lennon R., Melby S. et al. Frequency and correlates of coronary stent thrombosis in the modern era: analysis of a single center registry. *J. Am. Coll. Cardiol.*, 2002, 40, 1567–1572.
33. Ong A.T., McFadden E.P., Regar E. et al. Late angiographic stent thrombosis (LAST) events with drug-eluting stents. *J. Am. Coll. Cardiol.*, 2005, 45, 2088–2092.
34. Chevalier B. et al. Randomized controlled trial between biolimus-eluted Nobori and paclitaxel-eluted Taxus coronary stents. *Eurointervention*, 2007, 2, 426–424.
35. Virmani R., Farb A., Guagliumi G., Kolodgie F. Drug-eluting stents: Caution and concerns for long-term outcome. *Coron. Artery Dis.*, 2004, 15, 313–318.
36. Blindt R., Hoffmeister K.M., Bienert H. et al. Development of a new biodegradable intravascular polymer stent with simultaneous incorporation of bioactive substances. *Int. J. Artif. Organs*, 1999, 22, 843–853.
37. Heublein B., Rohde R., Kaese V. et al. Biocorrosion of magnesium alloys: A new principle in cardiovascular implant technology? *Heart*, 2003, 89, 651–656.
38. Waksman R. Biodegradable Stents: They do their job and disappear. *J. Invasive Cardiol.*, 2006, 18 (2), 70–74.
39. Tsuji T., Tamai H., Igaki K. et al. Biodegradable stents as a platform to drug loading. *Int. J. Cardiovasc. Intervent.*, 2003, 5, 13–16.

# The Prospects of using Biodegradable Stents in Treatment of Atherosclerotic Vascular Diseases (Review of Literature)

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Among percutaneous coronary interventions (PCI), coronary stenting has become the basic method in treating patients with coronary heart disease. Coronary stents are used as frame devices which lift the main restrictions of balloon angioplasty and increase the safety of interventions by preventing an early elastic recoil and late remodeling of the vessel (1, 2, 3). At the same time, the role of stents is temporary and is limited to a relatively short period, starting since the moment of intervention and ending a few days after the PCI, when healing and re-endothelialization processes are completed at the site of injury. Therefore, a wide usage of stents has demonstrated that their permanent presence in the vessel causes thrombosis, chronic inflammation and neointimal proliferation, leading to restenosis. For standard bare metal stents (BMS), thrombosis significantly reduced after using two-component antithrombotic therapy; however, restenosis remained to be a significant problem. The rate of restenosis was significantly reduced after introducing drug-eluting stents (DES) in the clinical practice.

## Why is there a need for bioabsorbable stents?

Problems of bare metal stents can be solved by using bioabsorbable stents. Despite development and progress of bare metal stents, stent thrombosis remains a threatening complication. The mechanism of implanted stent consists in preventing narrowing of the vascular lumen due to a metal frame, which is associated with favorable late remodeling (4). However,

permanent bare metal stents impair the vessel geometry and often completely obstruct the side branches.

Introduction of drug-eluting stents (DESs) into the clinical practice significantly reduced the incidence of restenosis and the need for repeated interventions. Preliminary and subsequent prolonged antithrombotic therapy makes it possible to reduce the risk of thrombosis, and mismatch between the implanted stent and the size of unimpaired vessel often results in inadequate expansion of the lumen at the site of implanted stent. However, despite prolonged double antithrombotic therapy up to 12 months, percentage of subacute and late thrombosis remains rather high. Moreover, the polymer used as a vehicle for local drug delivery may induce vessel irritation, endothelial dysfunction, hyperreactivity of the vessel and chronic inflammation at the site of implantation (5). Excessive implantation of stents in the coronary vasculature with formation of extended metal constructions may interfere with subsequent necessary surgical procedures of myocardial revascularization. Besides, bare metal stents pose artifacts with modern non-invasive imaging technologies such as magnetic-resonance imaging and multispiral X-ray computed tomography which showed good results in non-invasive diagnostics of coronary atherosclerosis.

In contrast to bare metal stents, bioabsorbable stents, after being completely eliminated from the vessel, leave behind only an expanded vascular lumen, allowing restoration of vasoreactivity with potential vascular remodeling. Late stent thrombosis is also unlikely in a situation when the stent is gone from the vascular lumen, which does not require prolonged antithrombotic therapy. Bioabsorbable stents are suitable for complex lesions where the stents may significantly impede on vascular geometry and may crush and fracture, in particular, in subcutaneous tibial and femoral arteries. Moreover, bioabsorbable stents may

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## Characteristics of biodegradable polymers and alloys

Polymer	Melting point, °C	Degradation time, months
Poly-L-lactic acid (PLLA)	173–178	>24
Polyglycolic acid (PGA)	225–230	6–12
Poly (D, L-lactide/glycolide) copolymer (PDLA)	amorphous	12–16
Polycaprolactone (PCL)		>24
Magnesium alloy		1–3

deliver drugs or genes, and perhaps play a role in treatment of unstable plaques. Transferring genes that code the cell proliferation pathway with the help of stents seems to be a promising method. Regardless of the impact of delivered agent (drug or gene) on restenosis, polymeric stents are the most suitable for such kind of delivery. Moreover, bioabsorbable stents are compatible with MRI and multispiral computed tomography (MSCT).

### Polymeric stents for local drug and gene delivery

Polymeric stents have the potential for local delivery of drugs and genes. Polymeric material, especially biodegradable polymers, are widely used for controlled (adjustable) drug delivery (6, 7, 8, 9). It is possible that designed biodegradable polymeric coatings of the stents will not only be a physical barrier between the vessel wall and the stent, but also will pharmacologically prevent thrombus formation and neointimal proliferation. Such biopolymers are currently loaded on the bare metal stents and deliver genes or drugs. After completing their mission, they (polymers) undergo complete degradation and leave only the metal stent itself contacting with the vessel wall.

### Bioabsorbable polymers and stent design

There are several requirements for selecting a polymer or alloy for bioabsorbable stent. They include the strength of the polymer to avoid possible immediate recoil, the rate of degradation and corrosion, biocompatibility with the vessel and no toxicity. The change in the mechanical properties and the profile of drug release from bioabsorbable stents may heavily depend on the rate of breakdown (degradation) of the stent itself. This affects the selection of the stent itself or alloy from which the stent is made, as well as passivation of eluting agent and the manufacturing process of the stent. Currently, two types of materials are being used for bioabsorbable stents: polymeric-based and metal-based.

Polymers are widely used in cardiovascular surgical devices and are used for local drug delivery (10, 11). Among the polymers used for bioabsorbable stents, the following are currently known: poly-L-lactic acid (PLLA), polyglycolic acid (PGA), poly (D, L-lactide/glycolide) copolymer (PDLA) and polycaprolactone (PCL). The degradation rates of these polymers are listed in the Table.

Each of the above listed polymers was designed for either self-expanding or balloon-expandable stents. Another possible design of a hybrid stent is a stent which combines polymeric bioabsorbable components with metallic backbone to enable strength and to prevent early recoil.

Among the first polymeric stents, bioabsorbable PLLA stent was tested. It was designed and evaluated by Stack et al. (12). He reported about creating 1000 mmHg pressure without changes in the stent which maintained its radial strength for 1 month. This stent was completely degraded in 9 months with minimal rate of thrombosis, moderate neointimal growth and limited inflammatory response in porcine coronary arteries.

Another polymeric stent (Igaki-Tamai) was made of PLLA monofilament (with molecular mass = 183 kDa) with a zigzag helical coil design (Fig. 1).

Another interesting concept of the multilayered biodegradable stent was offered by Eury

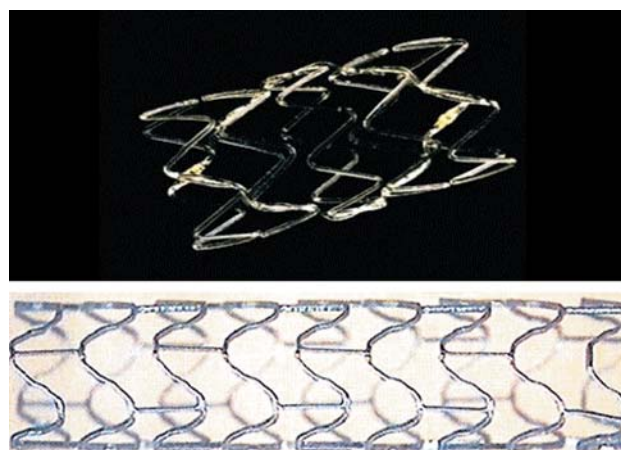


Fig. 1. The Igaki-Tamai PLLA monofilament stent.

et al. (13). It was made of combined PLLA, PGA, PCL, polyorthoesters and polyanhydrides. Unique features of this stent are that one of its layers creates the structure of the stent, and additional layers are responsible for elution of different drugs. The laminated construction allows few drugs to be simultaneously present in one stent, without interacting with each other. And drug release depends on the characteristics of the polymers-containers.

### Preclinical studies of polymeric stents

The initial experimental studies of biodegradable stents with PLLA, PCL, poly(hydroxybutyrate-hydroxyvalerate) and polyorthoester coated as films on the whole surface of wire stents and implanted in the porcine coronary arteries were disappointing. In 30 days after implantation, histology studies revealed that these coatings provoked a significant inflammatory response, neointimal proliferation and extensive cell infiltration, first of all, by multinucleated giant neutrophils, leukocytes, lymphocytes, monocytes and eosinophils. In addition to these processes, medial necroses were detected and pseudoaneurysms were also formed (14). Lincoff et al. (15) demonstrated that low molecular weight PLLA is associated with pronounced inflammatory reaction, and minimal inflammatory activity occurred with high molecular weight PLLA.

When comparing the Igaki-Tamai stent with the Plamaz-Schatz stent, there were no differences in the rate of thrombosis and in the minimal lumen loss after 6 months. Histological assessments revealed no significant inflammation and demonstrated minimal neointimal hyperplasia on PLLA structures (16).

Using a stent made of L- and D-lactide copolymer (L/D ratio was 96/4%), Hietala et al. (17) conducted a study in rabbits with 34-month follow-up. This is the longest known study which showed that complete endothelialization occurred after implantation of this polymeric stent in 3 months, with no inflammatory reactions observed within 6 months after stenting. Hydrolyzation of the stent was evident at 12 months, and complete disintegration – at 24 months. This stent was partially replaced by fibrosis elements. The vessel lumen remained patent throughout the whole observation period. In contrast to this observation, the Kyoto University bioabsorbable stent made of PGA and polyhydroxybutyrate was significantly associated with subsequent pronounced inflammatory reactions and thrombosis.

### Preclinical studies of polymeric stents for local drug delivery

Yamawaki et al. (8) included an antiproliferative agent into the high-molecular PLLA of the Igaki-Tamai stent. The stent was loaded with tranilast – ST638 (a specific tyrosine kinase inhibitor), or with ST494 (an inactive metabolite of ST368) and implanted in porcine coronary arteries. Histological analysis showed that the extent of neointimal formation was significantly smaller when the stent released an active ST368 as compared with inactive ST494, which did not impede neointimal growth and geometric vessel remodeling.

Vogt et al. (9) added paclitaxel to the stent made of poly (D, L)-lactic acid copolymer (PDLLA) and assessed the profile of drug release from the stent. They discovered an exponential pattern of paclitaxel elution rate and slow-release profile with initial level of 5–8 µg/day and subsequent decrease to 1 µg/day by 4 weeks and to 0 µg/day by 3 months. Generally, the stent demonstrated good mechanical stability. In 3 weeks after stenting, the histomorphometric analysis demonstrated inhibition of neointimal growth by 53% with paclitaxel elution from PDLLA stent as compared with PDLLA stent without the drug. Similar comparison with bare metal stent demonstrated reduction of neointimal growth by 44%. Such reduction of neointimal growth was observed until the 3rd month of follow-up.

In summary, these studies demonstrated the feasibility of coating/loading drugs in biodegradable stents with further actual inhibition of neointimal growth.

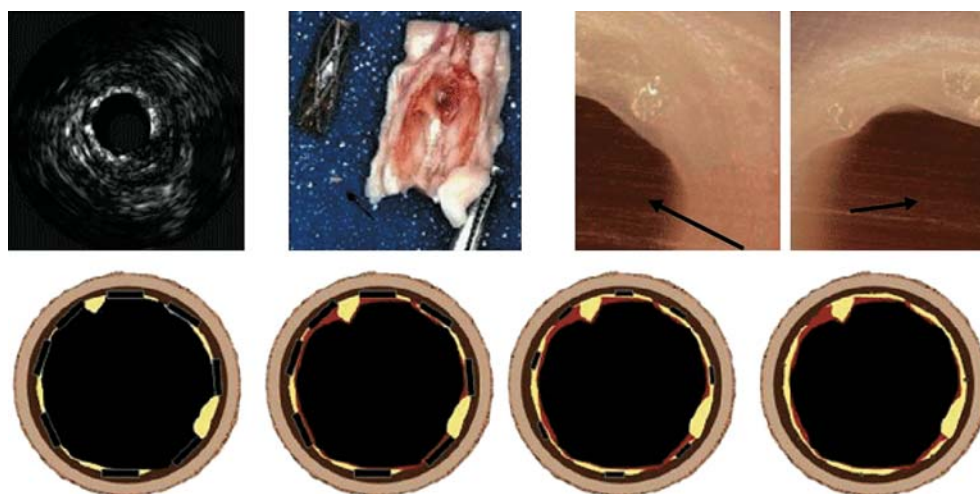
### Preclinical studies of polymeric stents for local gene delivery

Ye et al. (18,19) demonstrated a successful transfer and expression of a nuclear-localized β-Gal reporter gene in cells of the rabbit arterial wall. They used a PLLA/polycaprolactone stent impregnated with a recombinant adenovirus containing β-Gal reporter gene.

### Clinical studies with polymeric stents

Tamai et al. (20) were the first to report immediate and 6-month results after implanting the Igaki-Tamai polymeric stent in 15 patients. A total of 25 stents were implanted. The Igaki-Tamai stent was electively implanted in 19 impaired segments with 100% angiographic success. The investigators conducted clinical and angiographic follow-ups in 1 day, 3 months and 6 months. No stent thrombosis or pronounced





**Fig. 2.** Stages of elimination of magnesium stent from the vessel.

cardiovascular complications and events were observed within up to 30 days of follow-up. By 6 months, the rate of restenosis and subsequent revascularizations per lesion was 10.5%, and the rate per patient was 6.75%. The index of vascular lumen loss was 0.48 by 6 months, which encouraged the investigators. This study showed that the Igaki-Tamai stent is not associated with more pronounced neointimal growth as compared with stainless steel stents. When studying the vessel lumen with the help of intravascular ultrasound (IVUS), the increase of cross-sectional area from 7.42 mm<sup>2</sup> at baseline to 8.18 mm<sup>2</sup> at 3 months was observed.

Tsugi et al. (21) reported 1-year results of elective Igaki-Tamai stent implantation into 63 impaired segments in 50 patients. No angiographic and clinical complications were reported during hospitalization. Quantitative coronary analysis in 3, 6, and 12 months demonstrated an average percent diameter stenosis of  $12 \pm 8\%$ ,  $38 \pm 23\%$ , and  $33 \pm 23\%$ , respectively. The rate of significant restenosis was 21% (12 out of 58 patients) at 6 months and 19% (7 out of 36 patients) at 12 months. Repeat revascularizations of target segment were performed in 12% at 6 months and in 17% at 12 months. Up to 4-year follow-up demonstrated a long-term safety of this stent.

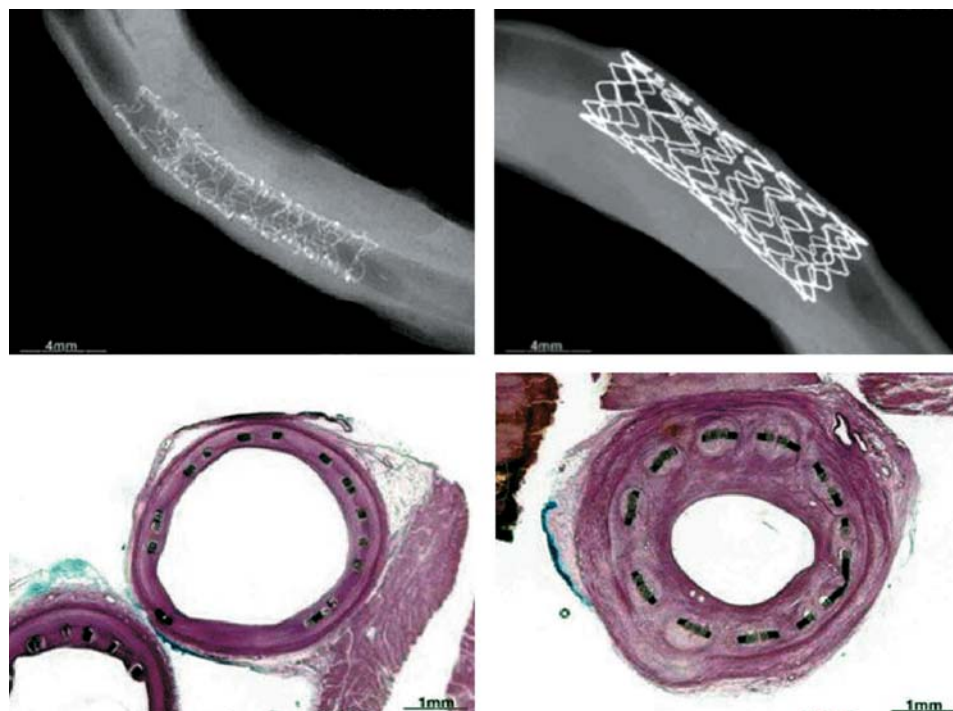
### Preclinical and clinical studies with bioabsorbable metal stents

Metal bioabsorbable stents have a potential comparable with stainless steel stents. Studies of their efficacy and safety in animals and humans are based exactly on this feature. Magnesium is the main bioabsorbable component of metal stents (Figure 2).

Magnesium is a rather attractive substance which can be bioabsorbed in the body. Heublein et al. (24) conducted a series of *in vitro* and *in vivo* preclinical trials with magnesium stents. Their studies demonstrated a high rate of complete stent degradation within 60–90 days since the moment of implantation with significant preservation of the stent in the vessel for 28 days. The stent had good biocompatibility with endothelial and muscle cells of the vessel. When comparing magnesium alloy stent with 316 L stainless steel stent in animals, positive vessel remodeling was observed for magnesium stents, with a reduction of neointimal growth and complete absorption of the stent within an interval from 30 to 56 days (Fig. 3).

The first clinical study of magnesium stents in patients was performed on peripheral vessels which were severely impaired (Rutherford Class IV and V), and the patients were candidates for limb amputation. Stents were placed in the popliteal arteries. Following predilatation, all  $3.0 \times 15$  and  $3.5 \times 15$  mm stents were successfully implanted with good angiographic and clinical results. No cases of toxic reactions to magnesium were observed. In 3 and 6 months after implantation the patency of the vessel was observed in 89% and 78%, respectively. All limbs were salvaged until 3 months, however by 6 months and 1 year there were single amputations due to progression of atherosclerosis. Duplex scanning showed complete absorption of stents at 3 months after implantation.

Results of this study encouraged the investigators regarding the prospects of using magnesium stents in the coronary vasculature. PROGRESS study was conducted at 7 European sites in 65 patients (25). IVUS demon-



**Fig. 3.** Comparison of magnesium stent with a 316L stainless steel stent in the porcine coronary artery 30 days after implantation.

strated complete absorption of implanted stents in 4 months; however, the restenosis rate was not that low.

Currently, there are ongoing research projects, which combine magnesium stents with local delivery of the drugs preventing restenosis. It turned out to be necessary, as relatively fast (30–60 days) disappearance of the stent from the vessel triggers subsequent inflammatory reaction and neointimal proliferation. Therefore, if the stents coated with antiproliferative agents slow or stop inflammation and neointimal growth, then optimal results may be achieved in coronary revascularization with magnesium used as a platform.

## References

1. Fischman D., Leon M., Baim D., et al. A randomized comparison of coronary stent placement and balloon angioplasty in the treatment of coronary artery disease. The STRESS Trial. *N. Engl. J. Med.*, 1994, 331, 496–501.
2. Serruys P.W., de Jaegere P., Kiemeneij F., et al. for the BENESTENT Study Group. A comparison of balloon expandable stent implantation with balloon angioplasty in patients with coronary artery disease. *N. Engl. J. Med.*, 1994, 331, 489–495.
3. Savage P.M., Fischman D.L., Schatz R.A., et al. Long-term angiographic and clinical outcome after implantation of a balloon-expandable stent in the native coronary circulation. *J. Am. Coll. Cardiol.*, 1994, 24, 1207–1212.
4. König A., Schiele T.M., Rieber J., et al. Influence of stent design and deployment technique on neointima formation and vascular remodeling. *Z. Kardiol.*, 2002, 91(Suppl 3), 98–102.
5. Virmani R., Farb A., Guagliumi G., Kolodgie F.D. Drug-eluting stents: Caution and concerns for long-term outcome. *Coron. Artery Dis.*, 2004, 15, 313–318.
6. Tsuji T., Tamai H., Igaki K., et al. Biodegradable stents as a platform to drug loading. *Int. J. Cardiovasc. Intervent.*, 2003, 5, 13–16.
7. Blindt R., Hoffmeister K.M., Bienert H., et al. Development of a new biodegradable intravascular polymer stent with simultaneous incorporation of bioactive substances. *Int. J. Artif. Organs*, 1999, 22, 843–853.
8. Yamawaki T., Shimokawa H., Kozai T., et al. Intramural delivery of a specific tyrosine kinase inhibitor with biodegradable stent suppresses the restenotic changes of the coronary artery in pigs in vivo. *J. Am. Coll. Cardiol.*, 1998, 32, 780–786.
9. Vogt F., Stein A., Rettmeier G., et al. Long-term assessment of a novel biodegradable paclitaxel-eluting coronary polylactide stent. *Eur. Heart J.*, 2004, 25, 1330–1340.
10. Hastings G.W. (Ed). *Cardiovascular Biomaterials*. Springer-Verlag: London, 1992.
11. Murphy J.G., Schwartz R.S., Huber K.C., Holmes D.R. Jr. Polymeric stents: Modern alchemy or the future? *J. Invasive Cardiol.*, 1991, 3, 144–148.
12. Stack R.E., Califf R.M., Phillips H.R., et al. Interventional cardiac catheterization at Duke Medical Center. *Am. J. Cardiol.*, 1988, 62(Suppl F), 3F–24F.
13. Eury K.R. Multi-layered biodegradable stent and method for its manufacture. European Patent 604022 A1.
14. van der Giessen W., Lincoff M., Schwartz R., et al. Marked inflammatory sequelae to implantation of biodegradable and nonbiodegradable polymers in porcine coronary arteries. *Circulation*, 1996, 94, 1690–1697.

15. Lincoff A.M., Furst J.G., Ellis S.G., et al. Sustained local delivery of dexamethasone by a novel intravascular eluting stent to prevent restenosis in the porcine coronary injury model. *J. Am. Coll. Cardiol.*, 1997, 29, 808–816.
16. Tamai H., Igaki K., Tsuji T., et al. A biodegradable poly-L-lactic acid coronary stent in porcine coronary artery. *J. Interv. Cardiol.*, 1999, 12, 443–450.
17. Hietala E.M., Salminen U.S., Stahls A., et al. Biodegradation of the copolymeric polylactide stent: Long-term follow-up in a rabbit aorta model. *J. Vasc. Res.*, 2001, 38, 361–369.
18. Ye Y.W., Landau C., Willard J.E., et al. Bioresorbable microporous stents deliver recombinant adenovirus gene transfer vectors to the arterial wall. *Ann. Biomed. Eng.*, 1998, 26, 398–408.
19. Ye Y.W., Landau C., Meidell R.S., et al. Improved bioresorbable microporous intravascular stents for gene therapy. *ASAIO J.*, 1996, 42, M823–27.
20. Tamai H., Igaki K., Kyo E., et al. Initial and 6-month results of biodegradable poly-L-lactic acid coronary stents in humans. *Circulation*, 2000, 102, 399–404.
21. Tsuji T., Tamai H., Igaki K., et al. One year follow-up biodegradable self-expanding stent implantation in humans. *J. Am. Coll. Cardiol.*, 2001, 37(Abstr), A47.
22. Tsuji T., Tamai H., Igaki K., et al. Biodegradable polymeric stents. *Curr. Interv. Cardiol. Rep.*, 2001, 3, 10–17.
23. Peuster M., Wohlsein P., Brugmann M., et al. A novel approach to temporary stenting: Degradable cardiovascular stents produced from corrodible metal-results 6–18 months after implantation into New Zealand white rabbits. *Heart*, 2001, 86, 563–569.
24. Heublein B., Rohde R., Kaese V., et al. Biocorrosion of magnesium alloys: A new principle in cardiovascular implant technology? *Heart*, 2003, 89, 651–656.
25. Waksman R. Biodegradable Stents: They Do Their Job and Disappear. *J. Invasive Cardiol.*, 2006, 18(2), 70–74.

## **70<sup>th</sup> Anniversary of Dr. David losseliani**



**The Editorial Board and the Editorial Council of International Journal of Interventional Cardioangiology present their cordial congratulations to the Editor-in-Chief, Corresponding Member of Russian Academy of Sciences, Head specialist on endovascular methods of diagnosis and treatment of Moscow, Director of Moscow City Center of Interventional Cardioangiology**

**David losseliani on his 70<sup>th</sup> birthday.**

**On this beautiful occasion we wish David losseliani strong health, new achievements in his scientific and practical activities, happiness and a lot of successes in all his undertakings!**