ISSN 1727-818X

International Journal of Interventional Cardioangiology

№31
2012

Read in the Journal:

RUSSIAN SOCIETY OF INTERVENTIONAL CARDIOANGIOLOGY

ISSN 1727-818X

INTERNATIONAL JOURNAL OF INTERVENTIONAL CARDIOANGIOLOGY

№ 31-2012

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

Website: www.ijic.ru

Address of the Editions:
101000, Moscow,
Sverchkov per., 5
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Fax (+7 495) 624 67 33

Scientific editor of translations:
V.S. Chekanov

Translation:
Translation bureau
MEDTRAN

Prepared by:
VIDAR Publishing House

Computer makeup:
Yu. Kushel

Corrector:
N. Sheludiakova

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

ISSN 1727-818X

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Contents

Endovascular Hemostasis in Pulmonary Hemorrhage

A.I. Kvashin, S.A. Atamanov, A.V. Melnik, A.O. Bykov, A.A. Pomkin, M.G. Shirkin, A.F. Portnyagin, F.N. Pacherskikh, E.G.Grigoriev*

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From 1974 till June 2012, bronchial arteriography (BAG) was performed in 1449 patients with pulmonary hemorrhage aged from 7 to 96 years old. Endovascular occlusion of bronchial arteries (EOBA) was performed in 1436 observations, endovascular occlusion of pulmonary artery (PA) branches – in 47 cases. Algorithm of therapeutic and diagnostic measures and classification of pulmonary hemorrhages have been developed. Angiographic signs have been systematized for the various nosologies. Immediate effectiveness of EOBA was 94.4%. Pulmonary hemorrhage (PH) recurred in 14.9% of patients in the immediate postoperative period and in 17.8% during the remote period. Diagnostic arteriography allows us to specify the nature of the underlying disease, to determine specific source of the bleeding. Endovascular occlusion of bronchial arteries and pulmonary artery branches is a highly effective, minimally invasive method of treatment of pulmonary hemorrhage.

Key words: *pulmonary hemorrhage; bronchial artery; endovascular occlusion; extravasation.*

Materials and methods. From 1974 till June 2012, bronchial arteriography (BAG) was performed in 1449 patients with pulmonary hemorrhage aged from 7 to 96 years old. Endovascular occlusion of bronchial arteries (EOBA) was performed in 1436 observations, endovascular occlusion of PA branches – in 47 cases. Algorithm of therapeutic and diagnostic measures and classification of pulmonary hemorrhages have been developed. Angiographic signs have been systematized for the various nosologies.

Results. Immediate effectiveness of EOBA was 94.4%. PH recurred in 14.9% of patients in the immediate postoperative period and in 17.8% during the remote period. The main cause of PH development was lung abscess (19.06%) We observed the following complications: thoracic pain syndrome – 82%; dysphagia – 3.2%; bronchial artery or aortic dissection – 0.6%; Brown-Sequard syndrome – 0.06%.

Conclusion. Diagnostic arteriography allows us to specify the nature of the underlying disease, to determine specific source of the bleeding. Endovascular occlusion of bronchial arteries and pulmonary artery branches is a highly effective, minimally invasive method of treatment of pulmonary hemorrhage.

Introduction

Pulmonary hemorrhage (PH) is caused by a deep damage of bronchial and pulmonary structures due to the pathological process (7, 8). The severity of condition and unfavorable outcomes during the massive ongoing PH are determined by respiratory failure as a result of blood aspiration in the intact parts of the lungs and development of asphyxia (1, 2, 7, 9, 24).

Conservative treatment of PH is associated with lethal outcome in 50%–100% of cases (13, 19). Surgical mortality rates vary between 7.1% and 18.2% and considerably increase (greater than 40%) in case of urgent surgery (14, 15). However, open procedures remain a method of choice in the treatment of PH, which occurred during the iatrogenic damage of pulmonary or bronchial arteries, chest injuries (18, 23).

Bronchoscopy is one of the primary methods of diagnostics and specification of PH localization. Nevertheless, diagnostic accuracy of bronchoscopy is less than 50% and depends on the hemorrhage activity and the degree of filling of the tracheobronchial tree with blood (16, 17, 18). Bronchoscopy in combination with endoscopic bronchial occlusion (EBO) restores the patency of airways, provides adequate ventilation, discontinues the blood inflow into the tracheobronchial tree (1, 3, 6, 7, 9). EBO is not a technique for immediate hemostasis, as it does not directly affect the bleeding vessel.

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The article was received on October 3, 2012.
Accepted for publication on December 17, 2012.

However, by stopping the hemorrhage into the bronchi of a healthy lung and preventing asphyxia, therapeutic tracheobronchoscopy provides the possibility to use one of the methods of final hemostasis in a relatively calm situation (5, 8).

Bronchial arteriography (BAG) and endovascular occlusion of bronchial arteries (EOBA) are minimally invasive and the most effective methods of diagnostics and cessation of PH of varying degrees and duration, which, as opposed to therapeutic endoscopy, allow us to locate a bleeding vessel, perform the final hemostasis, stabilize and prepare the patient for surgical treatment of the underlying disease (2, 4).

Materials and methods

Taking into account our professional experience, we offered a classification with 3 grades based on the blood loss per time unit. Moreover, the state of the tracheobronchial tree (patency) related to PH is taken into consideration in the classification. These parameters, from our point of view, are crucial in creation of complex therapeutic and tactical program, which includes the most rational and effective methods of diagnostics, therapy and surgery in a specific situation.

Fundamentally, PHs are classified as hemoptysis (Grade I), massive (Grade II) and profuse (Grade III) bleedings (Scheme 1).

From 1974 till 2012, bronchial arteriography (BAG) was performed in 1449 patients with pulmonary hemorrhage aged from 7 to 96 years old. In 1436 observations diagnostic catheterization was transformed into a therapeutic intervention on the systemic arteries, and in 47 cases endovascular occlusion of PA branches was conducted.

All interventions were conducted using Seldinger's femoral approach with 5 Fr introducer. During the 70s – 90s, a panel of variously modeled (depending on the nature of the study) self-made radioopaque catheters was used. Since 2000, JL 3.5–5.0 (MERIT MEDICAL) 5 Fr catheters have been used for selective and superselective catheterization of the PA. Recently, Cordis USL 2 modification has been used as a main catheter. For catheterization and implantation of metallic coils in the pulmonary artery branches we use Cordis MPA 2 modification. Any hydrophilic 0.035'' guide wires or chords for coronary angioplasty are used as guide wires for selective catheter placement.

In the 70s and 80s, methods of temporary hemostasis, such as blockage of the magistral blood flow using the tip of angiographic catheter and occlusion of peripheral branches by injecting macroaggregates of human serum albumin, and methods of irreversible hemostasis in the systemic pulmonary vessels (thrombosis of BA by administering irritant solutions (10% calcium chloride solution)) were used for endovascular hemostasis.

Scheme 1. Classification of pulmonary bleeding.

1st degree (hemoptysis)
- 1A – <50 ml/day
- 1B – 50–200 ml/day
- 1C – 200–500 ml/day

2nd degree
- 2A – 30–200 ml/hour
- 2B – 200–500 ml/hour

3rd degree
- 3A – ⩾100 ml at a time
- 3B – volume-independent asphyxia

X-ray endovascular occlusion of the bronchial artery (EOBA) or pulmonary artery branches with nonabsorbable materials (microporous polyurethane – polyurethane foam, teflon velour, Gianturco coils) were conducted in a majority of observations (70s – 90s). Flexibility and elasticity of polyurethane foam made it possible to implant emboli, exceeding in size the internal diameter of the catheter, which is important during the occlusion of hyperplastic BA in patients with bronchoectatic disease, polycystic lung disease and some other diseases. PVA particles and metallic coils of various modifications have been used as embolizing material since the beginning of a new millennium.

Results

Analysis of angiograms from patients with pulmonary hemorrhagic syndrome, reveals the direct and indirect signs of PH. Extravasation of contrasted blood and thrombosis of BA branches are the direct signs of hemorrhage and allow us to reliably locate the bleeding vessel. Indirect angiographic signs are not directly related to PH, but they rather fully characterize its cause, due to the specificity of semiotics of various pulmonary diseases. Extravasation of contrasted blood (194 patients – 13.3%) is a marker of ongoing bleeding; it occurs in the early arterial phase of opacification (Figure 1A). Depending on the massiveness of hemoptysis, a contrast spot may increase from 2 to 15 mm, reaching its maximal size during the parenchymatous phase (Figure 1B). Contoured bronchogram may be observed during the direct draining of blood into the airways (Figure 1C).

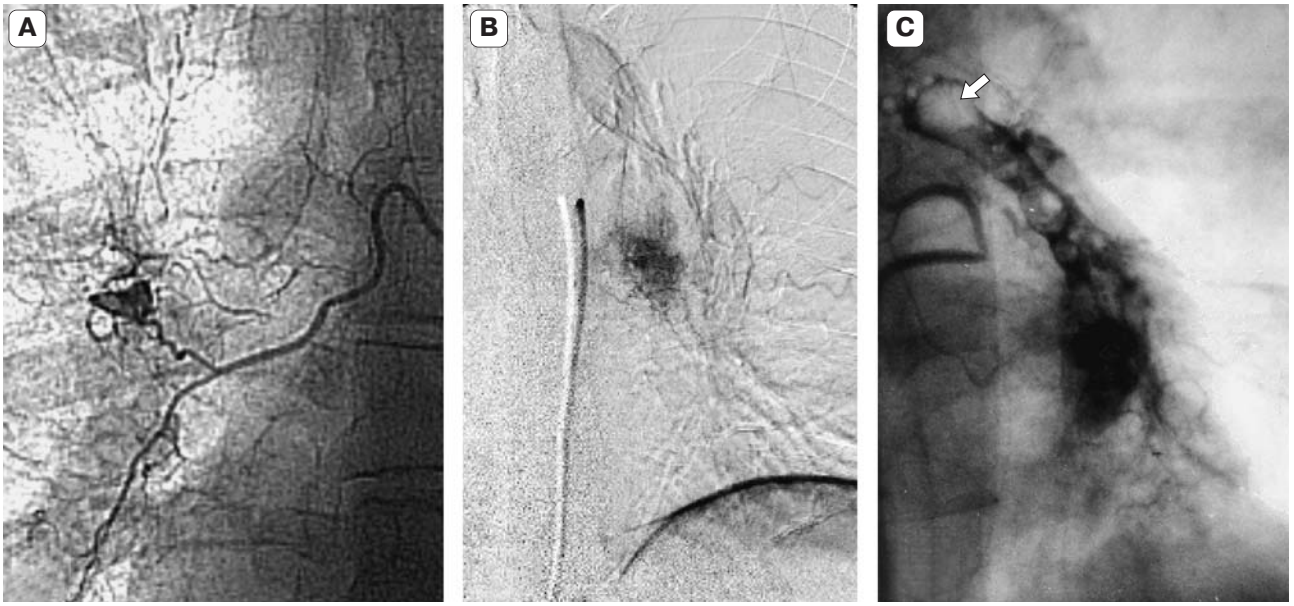


Fig. 1. (A) Early arterial phase of opacification. Extravasation in the territory of the right bronchial artery. (B) Long-standing retention of extravasated contrast medium (territory of the left bronchial artery). (C) Contour bronchography (polyurethane obturator in the ostium of the left main bronchus – arrow).

When analyzing the pattern of occurrence of this sign, we noticed one circumstance which initially could not be explained. Extravasation was certain in 11 (5.6%) patients; however, no hemoptysis was observed at that moment even with a provoked cough. After comparing data of angiography and endoscopy, we determined that segmental bronchi, draining the regions where the extravasates occurred, were occluded with solid, hardly removable blood clots. Thus, there was no contradiction between the appearance of a direct sign of PH and the absence of blood expectoration at that moment.

Thrombosis of bronchial artery branches (82 patients – 5.6%) is a direct angiographic sign of a recently stopped PH. On the angiograms, this symptom appears as a vessel "stump" (Figure 2A) with a wide base and serrate or denticulate contours. Symptom of periarterial diffusion of contrasted blood (280 patients – 19.3%), in our opinion, is the most informative among the indirect signs of PH. On the bronchial arteriogram, it manifests as the loss of vessel contours, local excessive suffusion of perivascular and peribronchial tissue with a contrast medium, and continuous retention of the contrast medium in the pathological region (Figure 2B).

Other indirect angiographic signs predominantly allow us to determine or specify the nature of the underlying disease, rather than reflect the presence or absence of pulmonary hemorrhage.

According to our data, the main cause of PH development was lung abscess (19.06%). The following was observed more rarely: bronchoectatic disease (18.11%); lung cancer (12.72%); pneumonia (11.56%); pulmonary tuberculosis (6.55%) and pulmonary gangrene (5.59%).

Angiographic semiotics in suppurative lung diseases has its own peculiarities: in the acute lung abscess, bronchial arteries are moderately tortuous, with usual or slightly increased diameter. We typically observe an increased peripheral bronchial circulation with a pronounced hypervascularization at the affected area in the arterial phase and long-lasting parenchymatous phase of opacification (Figure 3A).

On the contrary, magistral activation of systemic circulation is observed in the chronic lung abscess, resulting in a pronounced hyperplasia and tortuosity of magistral branches of the bronchial artery. Peripheral hypervascularization is less pronounced; precapillary arterioarterial shunting from the bronchial arteries to the branches of the pulmonary artery occurs (Figure 3B).

Pulmonary gangrene, chronic bronchitis and some types of chronic pneumonia are associated with a hypovascular type of blood supply (Figure 3C).

Angiographic semiotics of chronic inflammation is the most clear in bronchoectatic disease and complicated polycystic lung disease. Considerable hyperplasia of magistral arteries with a pronounced peripheral angiomatosis is observed. The volume of blood shunted through the precapillary bronchopulmonary bypasses is

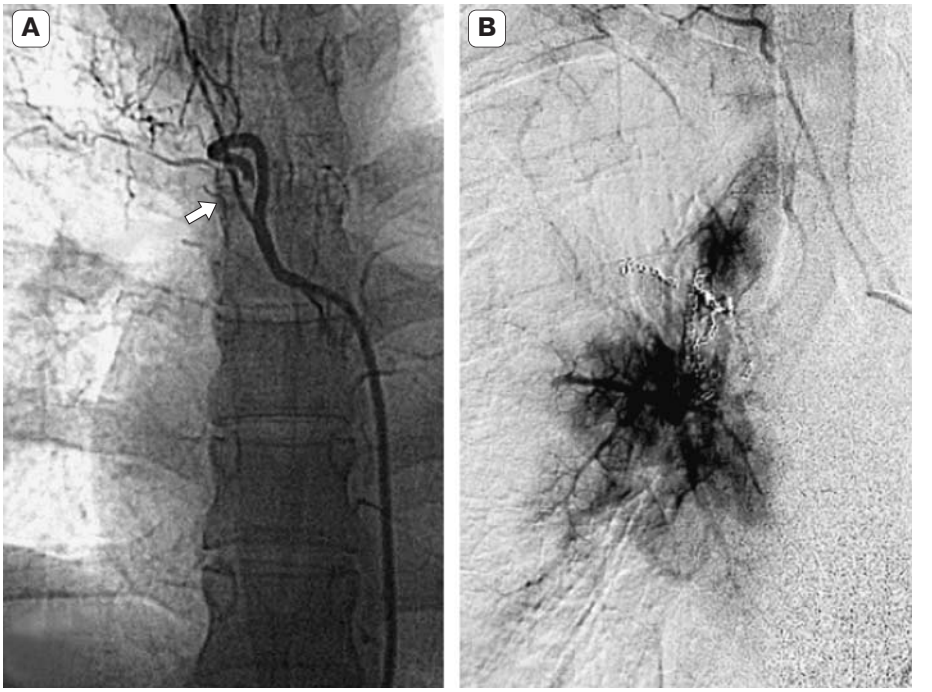


Fig. 2. (A) Thrombotic amputation of the bronchial artery in the territory of the right intercostal-bronchial trunk (arrow). (B) Symptom of periarterial diffusion with long-standing retention of contrast medium.

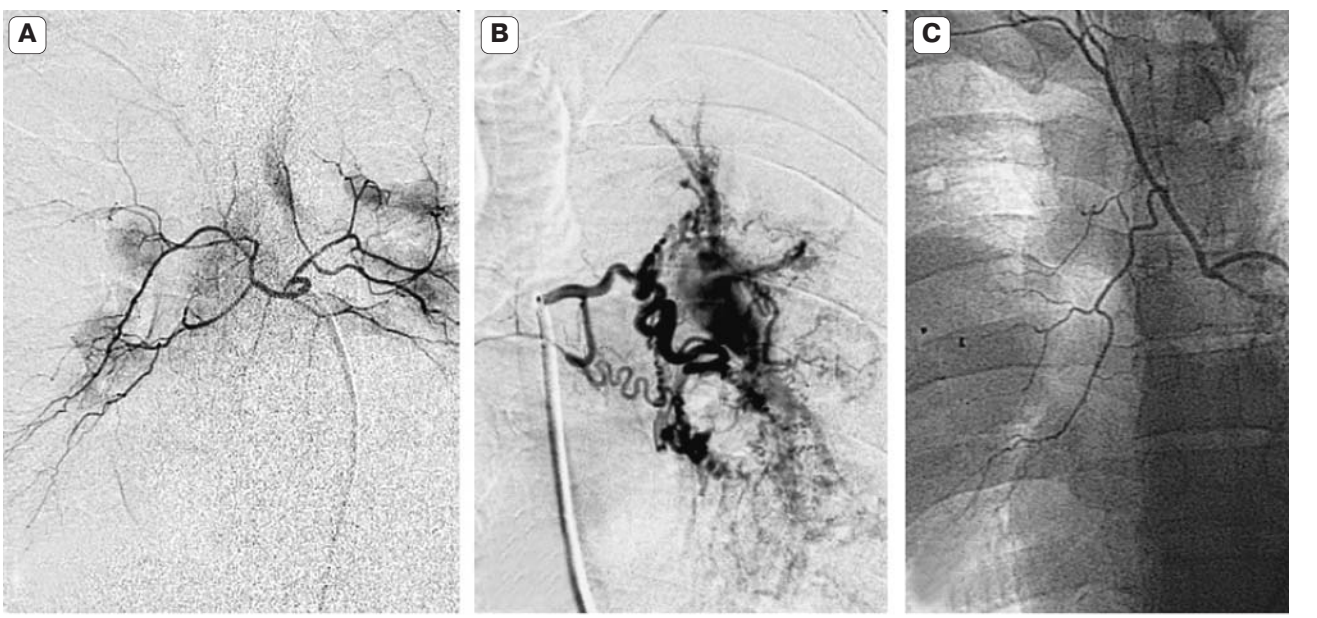


Fig. 3. (A) Activation of peripheral-type bronchial blood flow with extended parenchymal phase of opacification. (B) Marked tortuosity of the main trunk and atrerio-arterial shunting. (C) Hypovascular type of blood supply in lung gangrene. (D) Massive shunting with opacification of the lobular brabches of the pulmonary artery.

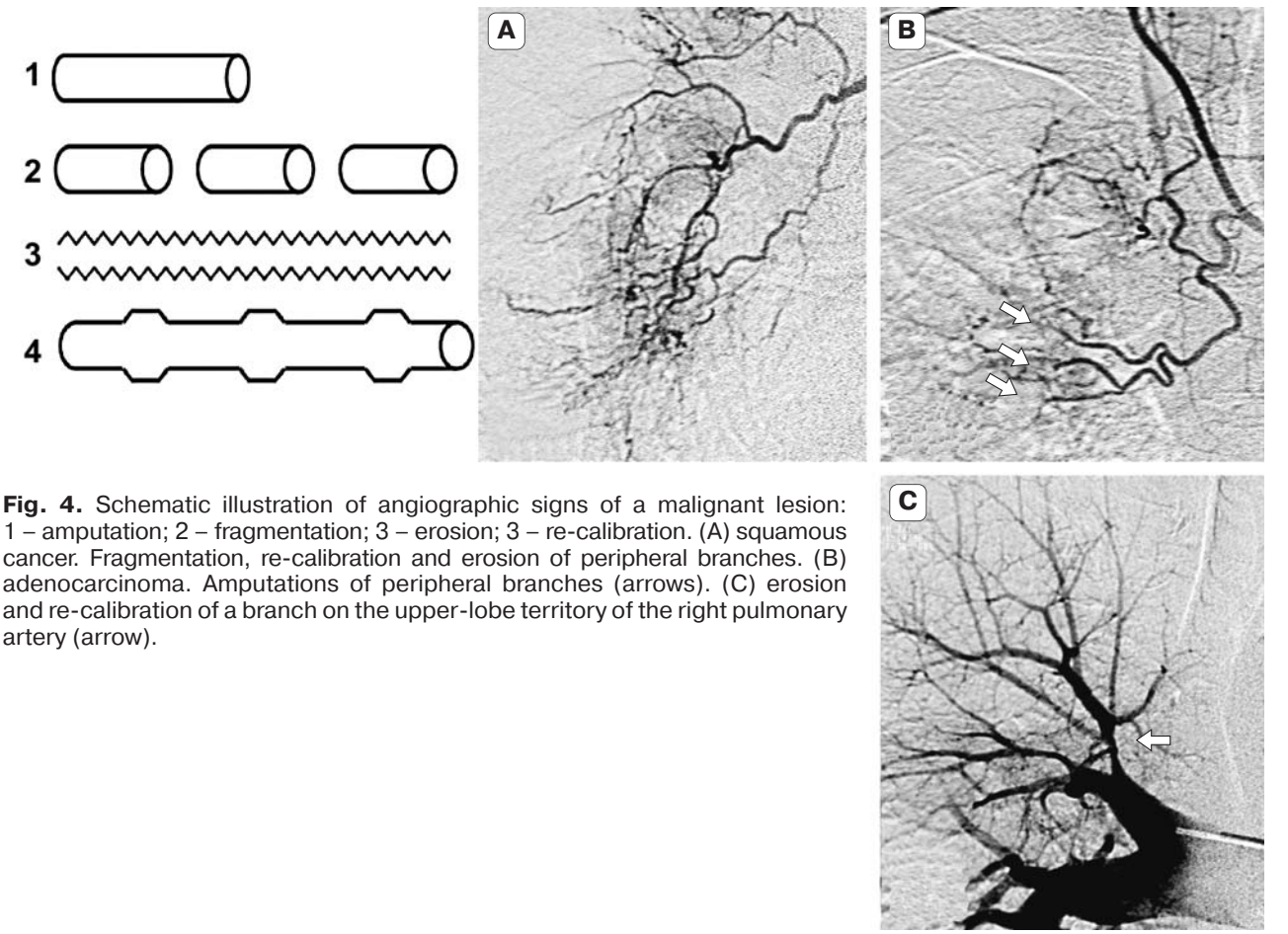


Fig. 4. Schematic illustration of angiographic signs of a malignant lesion: 1 – amputation; 2 – fragmentation; 3 – erosion; 3 – re-calibration. (A) squamous cancer. Fragmentation, re-calibration and erosion of peripheral branches. (B) adenocarcinoma. Amputations of peripheral branches (arrows). (C) erosion and re-calibration of a branch on the upper-lobe territory of the right pulmonary artery (arrow).

so pronounced that segmental, lobar and main branches of the PA are contrasted (Figure 3D).

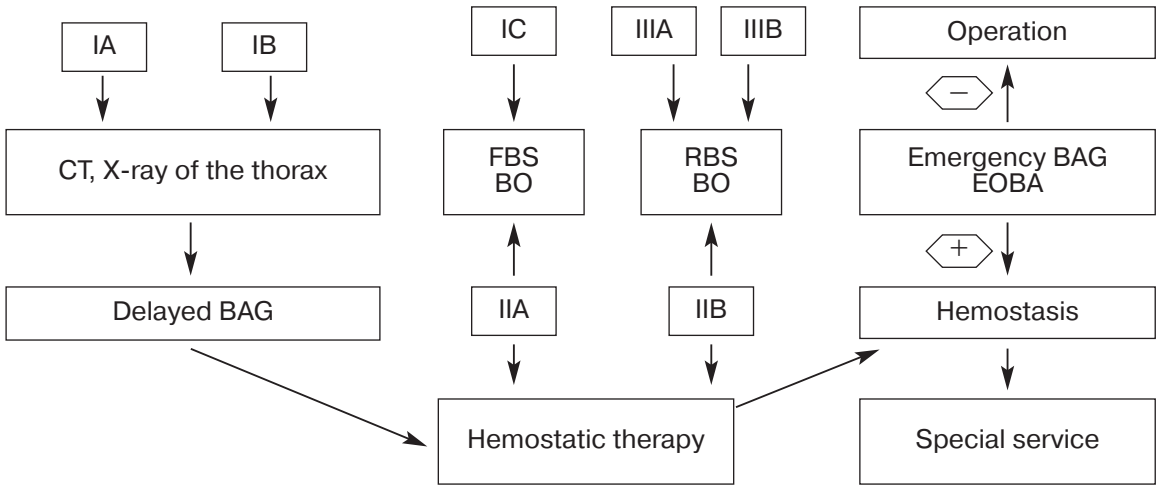
The tumor localization, its spreading and occurred complications affect the nature of angiographic changes in the lung cancer. The blood supply is depleted in the central lung cancer, but moderate peripheral hypervascularization may occur in case of obstructive pneumonitis. Cavernous form of the peripheral lung cancer, complicated by paracancerous pneumonia, is characterized angiographically by the hypervascular type of blood supply. Fragmentation of peripheral branches of the bronchial arteries is the most reliable angiographic sign, regardless of the blood supply type in the tumor. This sign, according to our data, is typical only for a malignant process, and it may be considered as pathognomonic for the lung cancer. Chaotic branching and distribution of bronchial artery branches with recalibration and amputation of the vessels, notching (serration) and smearing of the contours are observed in the tumor of hypervascular type (Figure 4A, B). If the tumor is rather large, the pulmonary artery may also be damaged, and the angiographic signs, typical for the malignant process, may appear (Figure 4C).

Thus, after analysis of angiograms, we were able to locate the bleeding source in the vast majority of observations (1223 patients (85.1%)), and to clarify the diagnosis of the disease in 1031 (71.2%) cases; in 31 patients (2.1%) the cause of PH remained unclear.

Urgent endoscopic investigation with obturation of the bleeding bronchus by polyurethane foam preceded the endovascular intervention. Differential approach towards the use of endovascular surgery, the principles of endovascular hemostasis, objectives and goals of the study were defined and specified while accumulating the experience.

In acute purulent-inflammatory lung diseases complicated by PH, it is appropriate to use such methods of treatment which, on one hand, stop the hemorrhage, and on the other hand, accelerate resolution of an acute inflammatory process. The latter, ultimately, is the most important for bleeding cessation and for preventing its recurrence.

Endovascular regional infusion therapy (ERIT) with occlusion of the BA orifice by the tip of catheter and with microembolization of peripheral vessels by the macroaggregated albumin (MAA) was used in the clinical settings



Scheme 2. Algorithm of therapeutic and diagnostic procedures depending on the intensity of pulmonary bleeding. CT – computed tomography; BAG – bronchial arteriography; FBS – fibrobronchoscopy; RBS – rigid bronchoscopy; BO – bronchus occlusion (polyurethane obturator); EOBA – endovascular occlusion of the bronchial arteries.

in the 70s – 80s. This procedure positively affected the course of the purulent-inflammatory process. As a matter of fact, this refers to the most rational route of administration of antibiotics, anti-inflammatory and some other drugs directly into the pathological focus.

Based on the detailed investigation of angiographic semiotics of pulmonary diseases and hemostatic performance of the reconstructive endoscopic surgery (RES) under study, we consider the use of ERIT to be optimal for the treatment of Grade I PH:

1. As complications of acute pulmonary suppurations;

2. In some cases of chronic abscess and bronchoectatic disease, if, according to BAG data, peripheral systemic circulation is preserved in the pathological area. Suggested type of endovascular hemostasis stopped hemoptysis in 80.33% of observations. PH recurred in 26.53% of patients and was arrested by the material EOBA.

Sclerosing endovascular therapy of Grade II and II A PH was forcedly conducted in 43 (2.9%) patients by administering calcium chloride (5.0–10.0 mL), when it was impossible to safely fix a catheter in the BA orifice. Administration of hypertonic fluids causes the vascular spasm, and their irritation effect on the intima results in endarteritis with subsequent thrombosis. As a result of conducted treatment, hemostatic effect was observed in 27 patients (62.79%); the endovascular procedure was ineffective in 16 patients (37.21%). Hemorrhage recurred in 11 patients (40.74%).

In terms of effectiveness and demonstrativeness of endovascular hemostasis, EOBA with nonabsorbable emboli has obvious advantages as compared with other methods. The world's first successful EOBA procedure was conducted by Remy et al. in 1974 (22). The first procedure in our clinic was conducted in 1976 by E.G. Grigor'ev. EOBA with nonabsorbable emboli has firmly settled in the treatment of PH and is used in the vast majority of cases. Until 2000, microporous polyurethane had been used as embolysate. COOK PVA 350–500 embolysate has been used since 2000.

Surgical endovascular hemostasis by embolizing systemic bronchial arteries was performed in 1436 patients (combined with the methods of therapeutic endovasal interventions in 39 of them). Algorithm of PH treatment has been developed in our clinic (Scheme 2).

Occlusion of the bronchial arteries was conducted:

1. In case of excessive hemoptysis (Grade 1 C), massive (2 A, B) and profuse (3 A, B) bleeding regardless of its cause and number of relapses;

2. In patients with chronic pulmonary suppurations and lung cancer, regardless of PH intensity;

3. In hemorrhagic syndrome caused by pathology of pulmonary systemic vessels, when no other cause of bleeding was revealed during a special study (idiopathic PH);

4. In recurrent PH, Grade I A and B.

Exclusion of all bronchial arteries, taking part in the blood supply of the pathologic region, is one of conditions of the reliable endovascular hemostasis, especially in patients with chronic pulmonary suppurations complicated by massive bleeding. Otherwise, the hemorrhage may

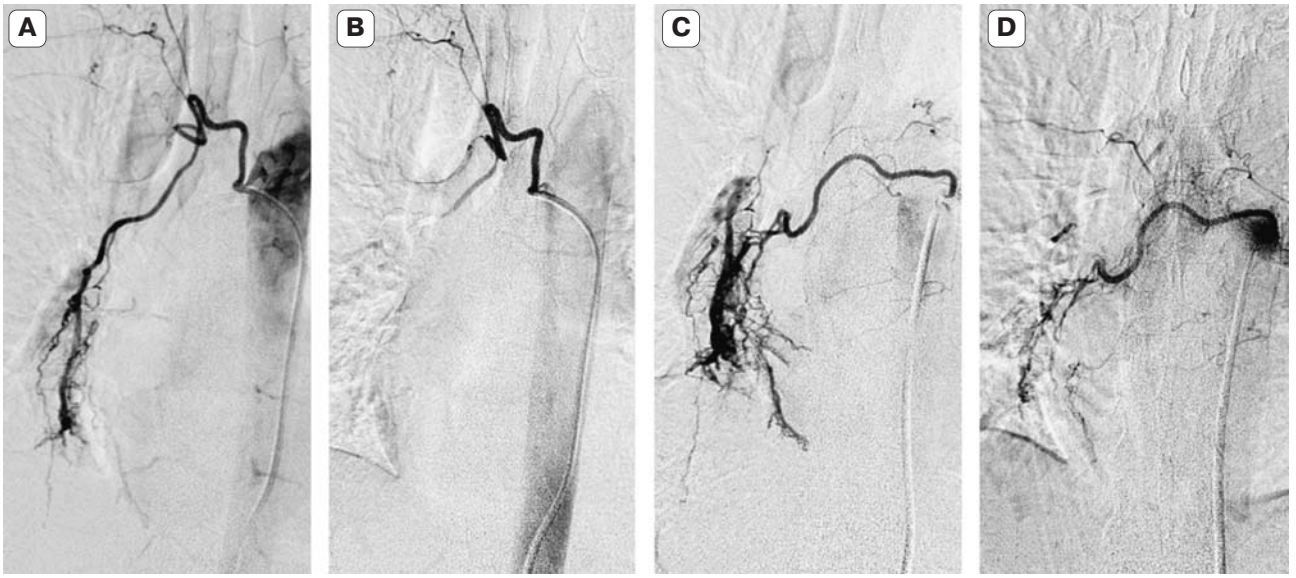


Fig. 5. (A) Extravasation, hypervascularization and arterio-arterial shunting in the territory of the right intercostal-bronchial trunk. (B) Sight after EOBA. (C) The same patient. The same signs in the territory of the right bronchial artery. (D) Sight after EOBA of the right bronchial artery.

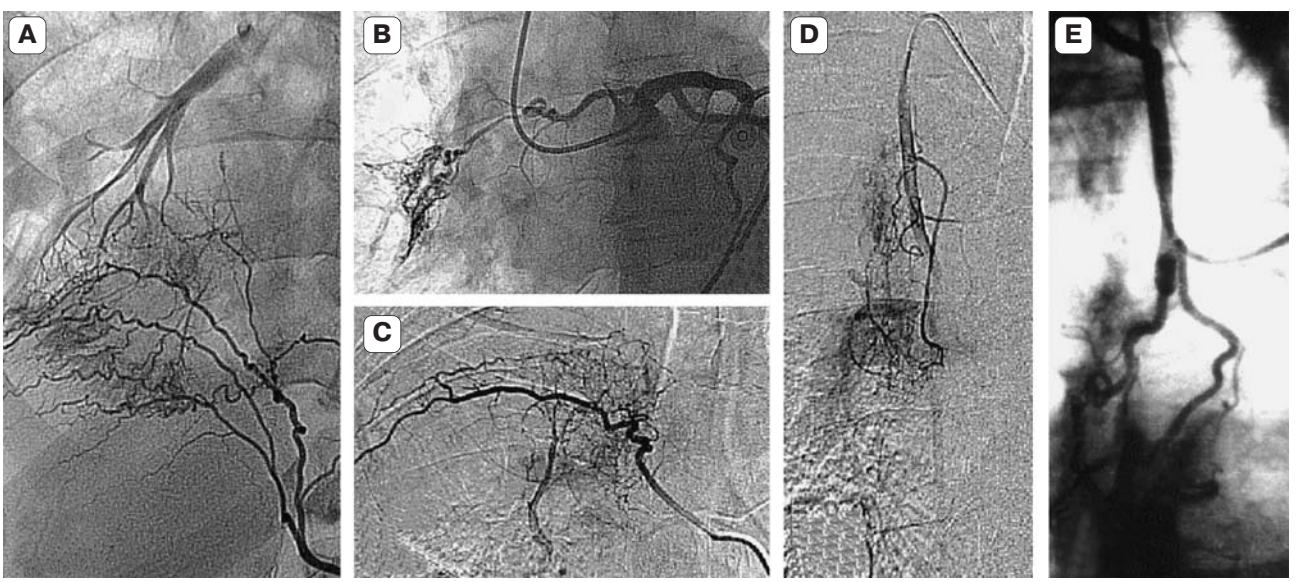


Fig. 6. (A) Aberrant artery from the territory of the left inferior diaphragmatic artery, massive arterio-arterial shunting. (B) Aberrant artery from the territory of the left coronary artery, signs of a chronic process. (C) Arterio-arterial shunting from the territory of the intercostal artery. (D) Aberrant artery from the territory of the internal mammary artery on the left. (E) Aberrant vessel from the territory of the left thyrocervical trunk.

relapse due to revascularization or to the damage of earlier non-occluded branches by the pathological process. According to our data, more than a half of PH relapses after EOBA occur exactly for this reason (Figure 5). The search, angiographic study and occlusion of abnormally arising aberrant BAs, whose orifices may be located in the different segments of aorta and its branches, cause well-known difficulties for the endovascular surgery of PH. In the clinic, catheterization and occlusion of the vessels, supplying or forming bypasses in the pathological area and originating from the thyrocervical trunk, coronary arteries, intercostals arteries, subclavian artery, celiac trunk, inferior thoracic and infradiaphragmatic segments of aorta were conducted (Figure 6).

During the working process, it has been determined that the pulmonary circuit vessels play an important and, probably, the leading role in the pathogenesis of PH in patients with gangrene, tuberculosis, lung cancer and arteriovenous aneurysms of the pulmonary artery. Thus, synchronous occlusion of BA and PA branches was performed in certain patients. Gianturco coils and COOK RMeye metallic coils were used

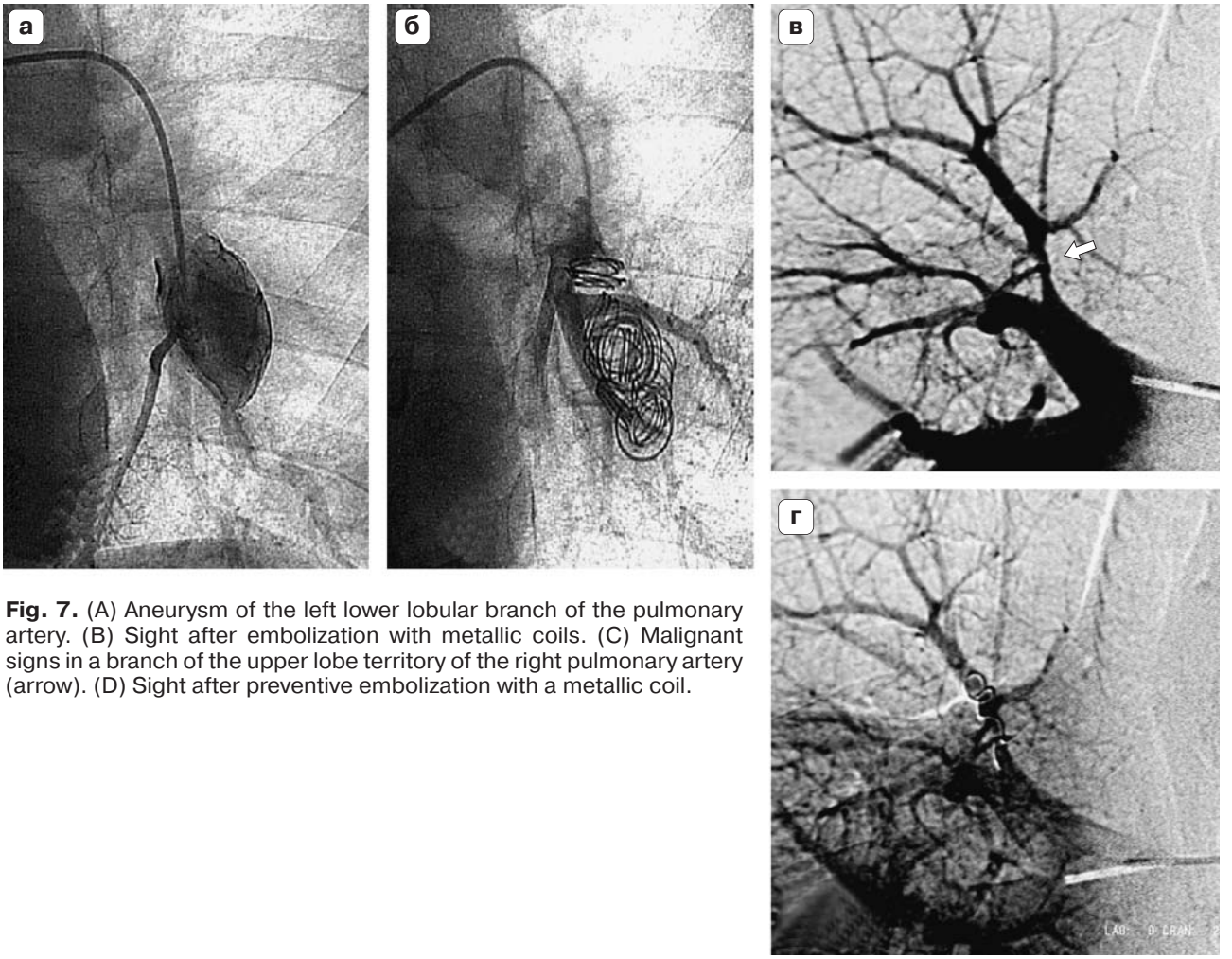


Fig. 7. (A) Aneurysm of the left lower lobular branch of the pulmonary artery. (B) Sight after embolization with metallic coils. (C) Malignant signs in a branch of the upper lobe territory of the right pulmonary artery (arrow). (D) Sight after preventive embolization with a metallic coil.

for embolization of PA branches. This procedure was performed in 42 patients (Figure 7).

Immediate effectiveness of the material EOBA was 94.4%; however, PH recurred in the immediate postoperative period (3 days) in 14.9% of patients. Hemorrhage recurred in 17.8% of observations in the remote period after material occlusion with the highest incidence in patients with chronic lung abscess, bronchoectatic disease and in patients with lung cancer who refused the surgery.

We observed the following complications during the conduction of endovascular hemostasis: thoracic pain syndrome – in 1188 (82%) patients; dysphagia – in 46 (3.2%); bronchial artery or aortic dissection – in 8 (0.6%); Brown-Sequard syndrome – in 1 patient (0.06%).

Discussion

Pulmonary hemorrhage has many etiological causes, varying in different parts of the world. Pulmonary tuberculosis and bronchoectatic disease are dominating in the eastern countries. Cancer, aspergillosis are the underlying causes of PH in the West. Popular causes are as follows: lung abscesses, pneumonia, pneumoconiosis, congenital heart and lung abnormalities, aneurysms of pulmonary artery and aorta (18).

Chest X-ray, computed tomography (CT) and bronchoscopy are three fundamental methods used to specify the localization of hemoptysis source. Chest X-ray is a simple, cheap and generally available diagnostic method; however, its diagnostic value is not high – it specifies the cause and localization of PH in 50% of cases (23). CT determines the cause and the source of PH with high accuracy (63–100%), it allows the X-ray surgeon to intentionally look for a bleeding vessel. Diagnostic accuracy of bronchoscopy is less than 50% and depends on the hemorrhage activity and the degree of filling of the tracheobronchial tree with blood (16, 17, 18). Bronchoscopy in combination with endoscopic bronchial occlusion (EBO) restores the patency of airways, provides adequate ventilation, discontinues the blood inflow into the tracheobronchial tree (1, 3, 6, 7, 9).

Success and effectiveness of EOBA procedure are related to a fair knowledge of bronchial

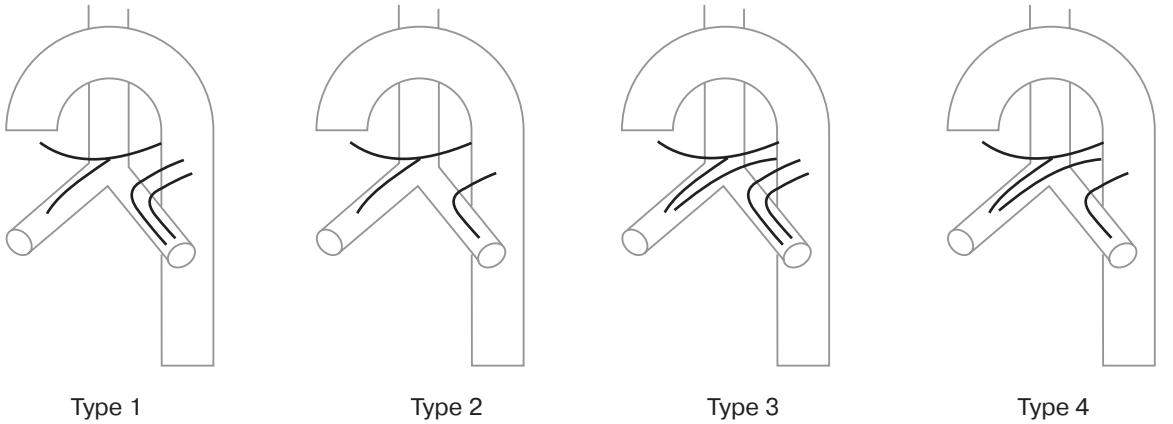


Fig. 8. Four main anatomic types of the bronchial arteries.
Type 1 – one right intercostal-bronchial trunk and two left bronchial arteries (40,6%). Type 2 – one right intercostal-bronchial trunk and one left bronchial artery (21,3%). Type 3 – one right intercostal-bronchial trunk, one right and two left bronchial arteries (20,6%). Type 4 – one right intercostal-bronchial trunk, one right and one left bronchial arteries (9,7%).

arteries (BA) anatomy by the operator, as these vessels are responsible for development of PH in 90% of cases (25). In 1948, Cauldwell et al. (11) created and systematized anatomic classification of BA, accentuating the 4 most common types of bronchial arteries (Figure 8). There are three types of bronchial arteries:

1) Systemic BAs arise from the anterior aortic semicircle between Th5 and Th6.

2) Abnormally arising BAs (aberrant) originate beyond the Th5–Th6 area. They originate from the aortic arch, internal thoracic aorta, thyrocervical trunk, intercostal arteries, inferior phrenic artery etc. They arise along (parallel to) the bronchi.

3) Systemic non-bronchial arteries – arteries, entering the lung parenchyma through pulmonary ligaments, pleural adhesions. Their direction is not parallel to the bronchi.

BA of the 2nd and 3rd group often cause the recurrence of PH in the early postoperative period (10–23%) (25). Overall incidence of PH relapses varies from 10% to 55.3% (12, 14, 21) and depends on the quality of the search for the pathologically changed arteries and aggressiveness of the underlying disease.

EOBA is minimally traumatic, highly effective and generally accepted method of hemostasis in PH of varying severity and etiology. Immediate hemostasis occurs in 88 – 100% of cases (10, 23). Method has its advantages over the surgical intervention, particularly in decompensated patients with pronounced pulmonary deficiency. EOBA makes it possible to avoid acute condition and stabilize the patient to perform subsequent surgical intervention for the underlying disease (23).

Currently, a variety of embolizing materials are used, such as metallic coils, gelatin sponge, PVA (polyvinyl alcohol) and glues. PVA with 350–500 μm particles is the recommended and most commonly used embolysate in the world, as it does not penetrate via the largest bronchopulmonary anastamoses, which size is about 325 μm (25). Proximal embolization of hypertrophied BAs with increased diameter or aberrants using only metallic coils is associated with the risk of “losing” distal collaterals, development of which may cause the recurrence of PH. Thus, spiral embolization in PH, as a rule, is combined with a dosed usage of PVA.

Thoracic pain syndrome (24–91%) and dysphagia (1–18%) are the most commonly described complications, occurring in accidental embolization of esophageal and intercostal branches. They are transient and resolve on their own during the immediate postoperative period (20). Transverse myelitis or Brown-Sequard syndrome (1.4–6.5%) is a serious complication, occurring during the embolization of anterior medullary artery (Adamkiewicz artery) or spinal arteries (20). Superselective catheterization of BA using microcatheter technique allows us to avoid this condition. Transverse myelitis was often observed in the 70s as a result of toxic effect of non-ionic contrast media. More rare complications include necrosis of the bronchus, pulmonary infarction, bronchoesophageal fistula (12).

Conclusion

Accumulated experience of diagnostic bronchial arteriography in patients with respiratory diseases allows us to consider it a leading

method of topical diagnostics of pulmonary hemorrhage, specifying the nature and peculiarities of the course of the underlying disease.

Endovascular selective reduction of bronchial vessels, and pulmonary artery branches in a number of cases, allows us to achieve immediate hemostasis in a vast majority of patients with pulmonary hemorrhagic syndrome, regardless of the nature of the pathological process. Combination of endoscopic bronchial occlusion with embolization of a bleeding artery minimizes the number of conventional surgical interventions at the peak of bleeding.

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Endovascular Hemostasis in Duodenal Hemorrhage

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From 1974 till May 2012, endovascular hemostasis was performed in 475 patients with gastroduodenal hemorrhage; 282 (59.3%) out of them underwent embolization of the gastroduodenal artery. A number of endovascular embolization techniques have been developed and implemented; angiographic signs of duodenal hemorrhage have been described and systematized. Sustained hemostasis of duodenal hemorrhage, originating from the gastroduodenal artery, was achieved in 91% of cases; hemorrhage recurred in 9%. Endovascular embolization of the gastroduodenal artery is a highly effective hemostatic technique in a group of patients with bleeding duodenal ulcer.
Key words: *gastroduodenal artery, embolization, extravasation.*

Introduction

Peptic ulcer disease causes more than a half of all gastrointestinal bleedings (8, 11). Timely diagnostic and therapeutic endoscopy allows to stop the bleeding in 98% of cases (5, 14). Despite this, mortality remains high (5–10%) in duodenal bleedings, which is, as a rule, related to the elderly age of the patients, concomitant diseases and, especially, the blood loss, requiring often multiple transfusions of blood elements (3).

Modern algorithm of treatment of duodenal bleedings (DB) is aimed at aggressive correction of coagulation and compensation of blood loss in combination with endoscopic hemostasis (2, 6). Injections of hemostatic agents, temperature exposures of the ulcer defect during endoscopy are reliable hemostatic techniques which, as a rule, are highly effective for recurrent DB as well. Acute bleedings which cannot be controlled conservatively or endoscopically account for about 5% of cases, requiring surgical or endovascular intervention (17). Mortality rate varies between 20–40% during surgical intervention at the peak of bleeding (4). Endovascular embolization in DB is considered as an alternative to the surgical intervention, especially for high-risk surgical patients, and is a leading diagnostic and treatment measure for endoscopically uncontrollable bleedings (1, 12, 15, 16). Moreover, endovascular occlusion of a bleeding vessel makes it possible to stabilize a patient and gain some time to prepare a patient for elective surgical intervention.

Mini-invasiveness, no general anesthesia, a wide choice of embolizing materials provide the endovascular DB treatment with a number of undeniable advantages as compared with traditional surgical approach.

Materials and methods

From 1974 till May 2012, endovascular hemostasis was performed in 475 patients with gastroduodenal hemorrhage; 282 (59.3%) out of them underwent this intervention for duodenal hemorrhage.

Hemodynamically unstable patients with ongoing massive bleeding, requiring transfusion of blood elements, resistant to conservative treatment and endoscopic hemostasis, were the candidates for endovascular intervention.

Opacification of the celiac trunk and superior mesenteric artery was conducted during the bleeding period or immediately following its cessation in 62.7% of patients and routinely in 37.3% of patients without hemorrhage.

The classic femoral approach was used in all observations. Celiacogaphy was performed, during which the anatomy of celiac trunk and its branches was specified, as well as the presence of ongoing bleeding. If there were no direct signs of bleeding, superselective catheterization of splenic, left gastric and gastroduodenal arteries was consecutively performed with further preventive "blind" embolization of a specified artery, according to endoscopic data.

Angiographic diagnostics was based on the detection of direct and indirect signs of hemor-

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Manuscript received on October 10, 2012.
Accepted for publication on December 17, 2012.

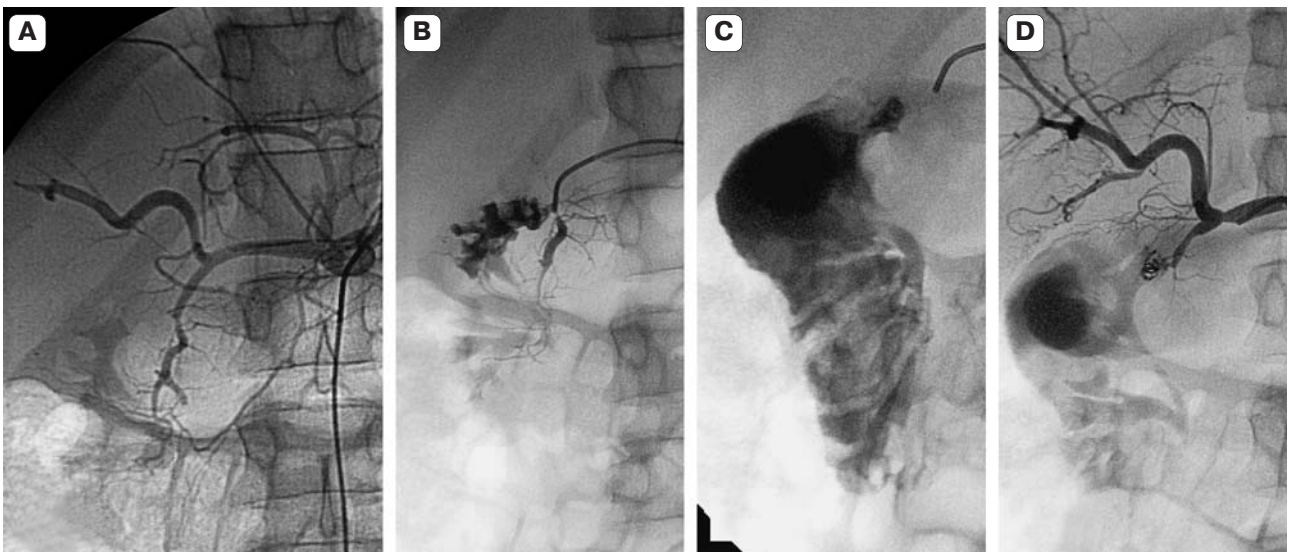

Figure 1. (A) Selective celiacography. Arterial phase of opacification. (B) Superselective catheterization of the gastroduodenal artery (GDA). Contrsat media extravasation into the lumen of the duodenal artery (DDA). (C) Contrast duodenography. (D) Image taken after coil embolization of the GDA.

rhage. The former signs (extravasation of contrasted blood, thrombotic vessel occlusion, regional arterial spasm, aneurisms of celiac trunk branches) absolutely and accurately detected the bleeding branch. The latter signs (local hypervascularization, periarterial diffusion of contrast-enhanced blood) reflected peculiarities of the main pathological process and located the source of DB with a known degree of reliability.

Three variants of endovascular interventions were performed:

1. Temporary blood flow reduction or cessation in the gastroduodenal arterial branches via infusion of vasopressor agents.

2. Combined angioreduction via temporary peripheral embolization with human serum albumin microaggregates during the infusion of vasopressor agents.

3. Superselective embolization of celiac trunk branches.

The first and second techniques of endovascular hemostasis were used in the clinics in the 70s and 80s.

X-ray endovascular occlusion of celiac trunk branches with nonabsorbable materials (microporous polyurethane – polyurethane foam, teflon velour, Gianturco coils) was conducted in a vast majority of observations. Polyvinyl alcohol (PVA) particles, metallic coils of various modifications have been used as embolizing material since the beginning of a new millennium.

Results

Contrast media extravasation was observed in 71 out of 282 (25.1%) patients. Extravasates of various forms and shapes were detected in the early arterial phase; their maximal size and intensity was achieved during the parenchymatous phase.

At the peak of bleeding, contrasted blood effused directly into the duodenal lumen, creating an impression of contrast duodenography (Figure 1).

When analyzing extravasate formation pattern, we noticed one circumstance requiring clarification. The fact of extravasal hemorrhage was certain in a number of patients; however, no inflow of the fresh blood from the stomach was observed at that moment with a functioning nasogastral probe. Gastric tamponade with thrombotic masses, detected during endoscopic examination, caused this.

Throughout all of our extravasation observations, this angiographic sign appeared, as a rule, during an active, massive or profuse duodenal bleeding (DB), when the hemorrhage coincided in time with opacification of a damaged vessel.

Thrombotic “amputation” of the gastroduoadenal artery was detected in 25 (8.8%) cases. This sign was never observed together with extravasation of contrasted blood. The vessel stump during an acute occlusion has a wide base and denticulated contours (Figure 2). The symptom under investigation in most of the patients was accompanied by prearterial diffusion of a contrast medium.

Regional arterial spasm was observed in 44 (15.6%) patients (Figure 3). In a vast majority of observations, vascular spasm was of occlusive nature. As opposed to thrombotic “amputation”, the stump contours of a spasmodic artery

resemble a cone with smooth well-defined contours. As in thrombosis, peripheral collateral vasculature is not marked. In 12 out of 44 patients with verified occlusive spasm, superselective catheterization was conducted in the basin of affected vessel with administration of spasmolytic agents. Extravasation was detected in 1 (8.3%) of them after opacification (Figure 3). Regional spasm is certainly a reliable sign of duodenal bleeding which directly points out the area of a damaged vessel. It may be combined with extravasation of a contrast medium after superselective catheterization or preliminary impact on the vascular tone.

Figure 2. Thrombotic "amputation" of the GDA.

Aneurysm of celiac trunk braches is a rare angiographic finding, which can also be interpreted as a direct sign of ongoing bleeding if revealed in the acute hemorrhage period – 4 (1.41%) patients (Figure 4).

Periarterial diffusion of contrasted blood (23.4%) is the most informative among the indirect signs of DB registered during the non-hemorrhagic period. As opposed to extravasation, periarterial diffusion is less intensive and does not have a well-defined border with surrounding tissues (Figure 5).

Local hypervascularization was the most common angiographic sign. It reflects the degree of inflammatory process in the pathologic region, assesses the nature of organic blood flow disorders, and in some cases, reflects the nature of the underlying pathology (Figure 5).

After analyzing angiograms, the localization of bleeding source was detected in 224 observations (79.4%).

Angiographic studies allowed us not only to localize the damaged vessel, but also to specify the nature of underlying pathological process in a number of cases.

Occlusive and pressure-occlusive techniques of DB hemostasis were applied in 98 (34.7%) patients in the clinical settings. However, hemorrhage recurred in a quarter of them.

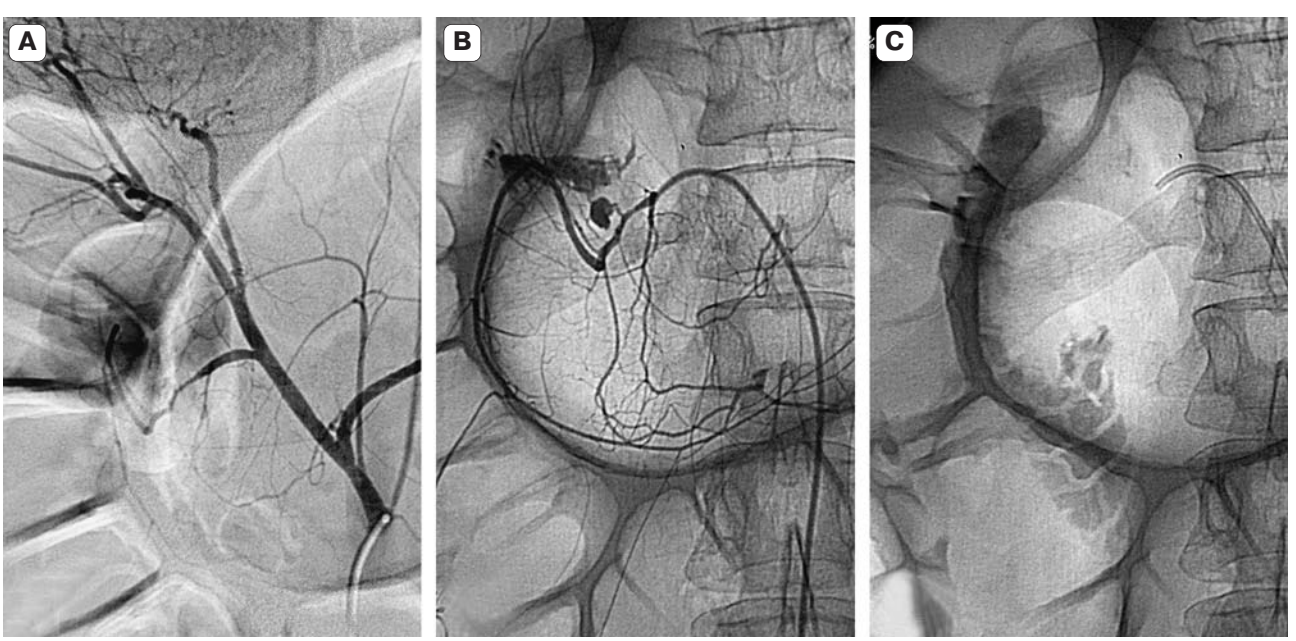

Figure 3. (A) Regional spasm of the GDA. (B) Spasm cessation and appearance of extravasation after the administration of spasmolytics. (C) Late phase of opacification. Contrast flow into the lumen of the DDA.

Angioreduction by nonabsorbable emboli was performed in 184 (65.2%) patients. Endovascular occlusion was conducted using microporous polyurethane, surgical felt, microspheres (PVA 500-700), coils of various modifications (COOK MReye Embolization coil, COOK MReye Flipper), hemostatic sponge and stent-graft. In 14 % of cases, it was impossible to conduct embolization due to various reasons (pathological tortuosity of aorta and iliacofemoral segments, insurmountable obstacles for superselective catheterization).

Good results of endovascular hemostasis were obtained after a total occlusion of the gastroduodenal artery in patients with bleeding duodenal ulcers. In a majority of observations

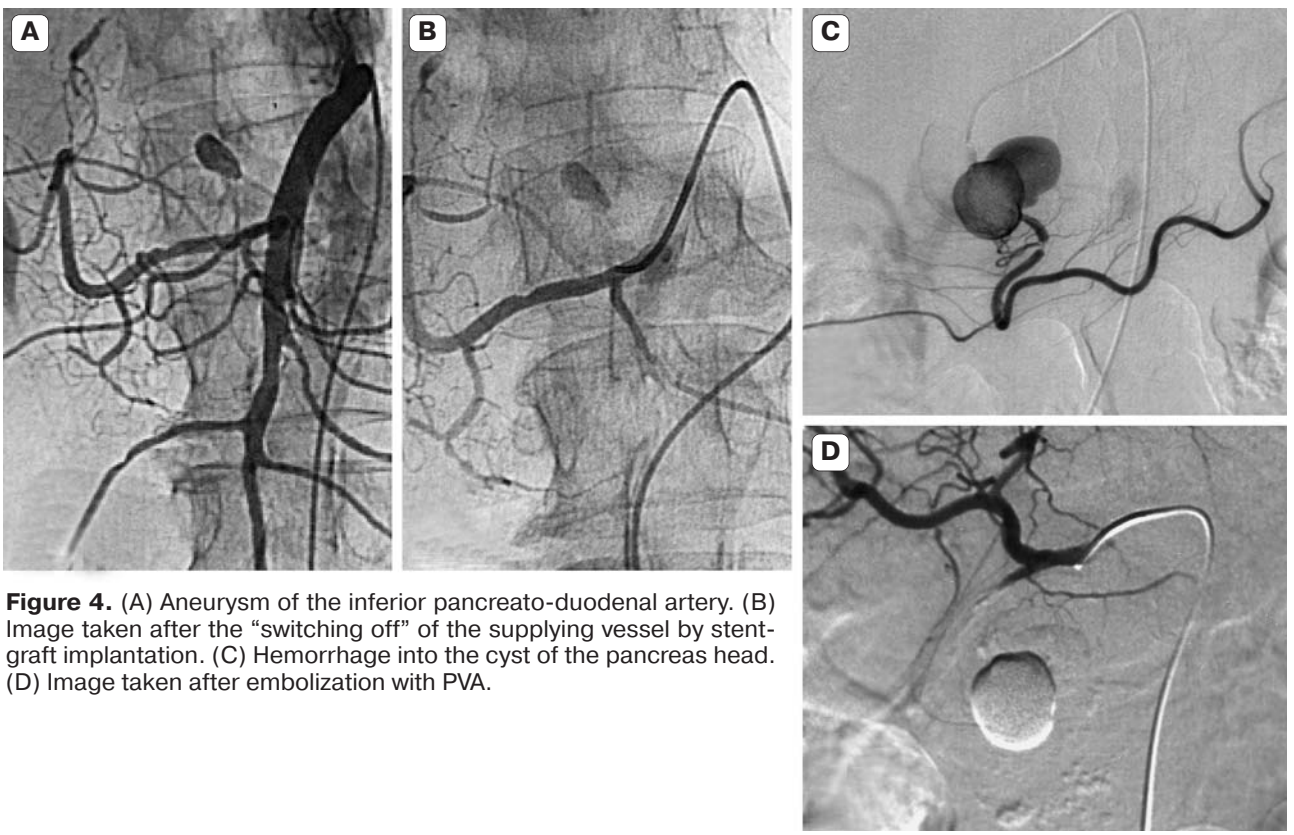

Figure 4. (A) Aneurysm of the inferior pancreato-duodenal artery. (B) Image taken after the "switching off" of the supplying vessel by stent-graft implantation. (C) Hemorrhage into the cyst of the pancreas head. (D) Image taken after embolization with PVA.

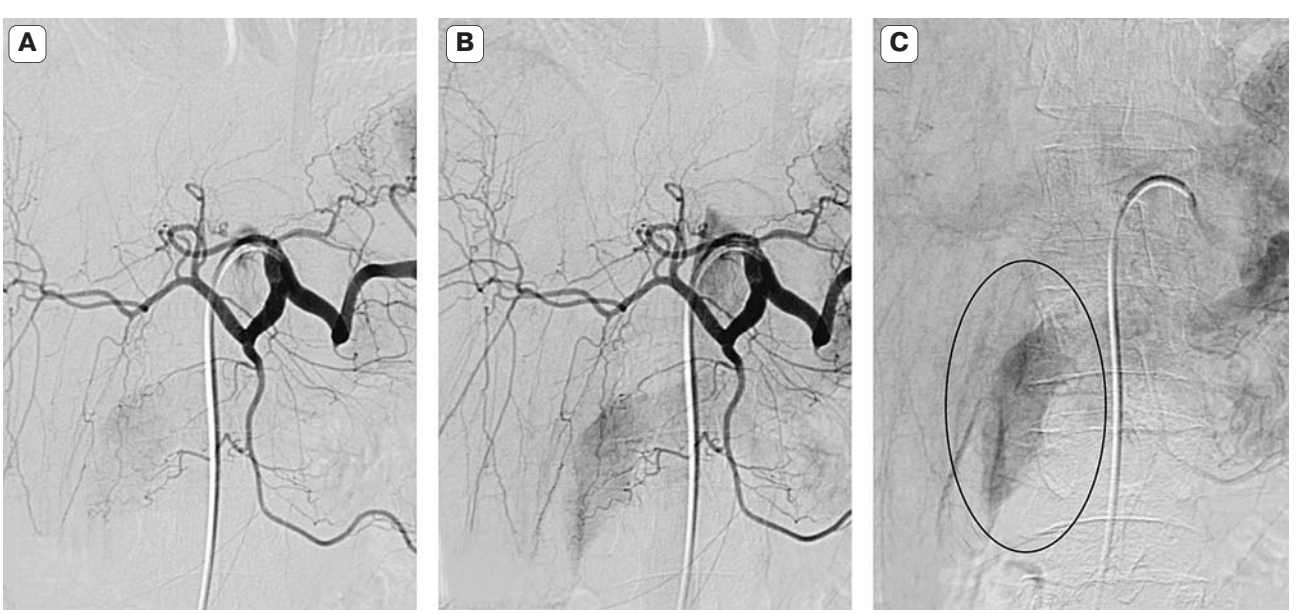

Figure 5. Local hypervascularization and periarterial diffusion with enhanced impregnation of the DDA mucosa during the parenchimatous phase. (A) Early arterial phase of opacification. (B) Late arterial phase of opacification. (C) Parenchimatous phase of opacification.

Table 1. Studies including the results of endovascular embolization of the GDA during the 17-years period (data from Loffroy et al., 2009)

Author, year	Patients (n)	Mean age (years)	Endoscopy (%)	Extravasation (%)	Technical success (%)	Clinical success (%)	Recurrence rate (%)	Operation necessary (%)	Complications (%)	30 days mortality (%)
Lang et al., 1992	57	52	NA	100	91	86	56	2	16	4
Toyoda et al., 1995	11	65	100	54	100	91	18	18	0	27
Toyoda et al., 1996	30	62	100	NA	100	80	23	13	NA	23
Walsh et al., 1999	50	64	100	50	92	52	52	37	4	40
De Wispelaere et al., 2002	28	69	100	39	89	64	36	21	0	46
Ljungdabl et al., 2002	18	78	72	50	72	67	8	8	0	6
Ripo U. et al., 2004	31	75	100	NA	100	71	29	16	0	26
Holme et al., 2006	40	70	100	30	100	65	28	35	0	25
Eriksson et al., 2006	10	75	100	10	100	80	0	20	NA	NA
Loffroy et al., 2008	35	71	100	66	94	94	17	14	6	21
Larssen et al., 2008	36	80	100	42	92	72	9	30	8	17
van Vugt et al., 2009	16	71	100	75	88	81	19	12	KA	38
Loffroy et al., 2009	60	69	100	63	95	72	28	12	10	27
All studies	422	69	98	53	93	75	25	18	4	25

(242 out of 282 patients – 86.8%), emergency surgical treatment was not required; moreover, none of the patients had clinical and endoscopic signs of duodenal or pancreatic ischemia.

Sustained hemostasis was achieved in a vast majority of patients (91%) with duodenal hemorrhage from the gastroduodenal artery; hemorrhage recurred in 9%.

Discussion

Rosch et al. were the first in the world to conduct endovascular embolization of the gastroduodenal artery (18). Currently, this procedure is a "gold standard" in diagnostics and treatment of endoscopically uncontrollable duodenal bleedings in patients at high surgical risk (9).

There are a number of studies devoted to endovascular control of DB in duodenal ulcer disease (Table 1). In 98% (89% in our observation) of cases, endoscopic hemostasis was ineffective, technical success rate was 93% (91% in our observation). Various embolysates were used: PVA, metallic coils, gelatin sponge, cyanoacrylate etc. "Sandwich" technique, involving embolization of distal and proximal (regarding the bleeding region) departments of the vessel, was often used to reduce the risk of DB recurrence by means of collaterals. Extravasation was observed in 53% of cases (25% in our study). Preventive "blind" embolization of the gastroduodenal artery was performed in case of no extravasation. DB recurred in about 25% (9% in our case) of patients during the immediate postoperative period, requiring surgery in 18% (13% in our case) of cases. Complications included complications at the site of access (hematomas, false aneurysms), dissection of a target vessel, hepatic or splenic infarction, duodenal stenosis – the most severe complication related to embolization of terminal muscle branches of the gastroduodenal artery, causing paresis of intestinal musculature. We did not observe such complications in our study except for a number of hematomas at the site of femoral artery puncture.

Mortality rate for DB varies from 17% to 43% among the patients, resistant to conservative therapy (10, 13). Elderly age, trauma, sepsis, preceding abdominal surgeries, massive hemotransfusions worsen the patient's condition (13,19). After embolization of the gastroduodenal artery, mortality rate varies between 10% and 45% among the patients at high surgical risk (19). Mortality rate in groups of patients with successful embolization and surgical intervention after unsuccessful embolization is 38% and 83%, respectively (7).

Timely and appropriate correction of coagulopathy is of special importance. Compromised coagulation increases the possibility of DB recurrence after a primary successful embolization of the gastroduodenal artery threefold and tenfold the mortality as a result of recurrent DB, as compared with patients with normal coagulation.

Conclusion

Endovascular occlusion of celiac trunk branches and, in particular, of gastroduodenal artery in acute duodenal bleeding allows us to achieve immediate hemostasis, to prevent rebleeding and to gain time for stabilization of patient's condition for elective surgery; in some cases, conservative therapy without surgical intervention is possible.

Embolization with nonabsorbable emboli and metal coils is the most effective method of final hemostasis in the gastroduodenal arterial hemorrhage.

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Recurrent Myocardial Infarction Caused by Simultaneous Thrombosis of the Stent and Second Coronary Artery in Patients with Multiple Coronary Lesions

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Simultaneous thrombosis of two coronary arteries or two stents implanted in different coronary arteries is possible in rare cases. In these circumstances, blood flow impairment occurs in a significant part of myocardium. Such condition requires immediate endovascular restoration of the lumen. We present two cases of simultaneous stent thrombosis in the left anterior descending artery (LAD) and obtuse marginal branch (OMB) 3 and 8 days after the primary intervention. Urgent endovascular surgery restored coronary blood flow in two arteries in one case and LAD blood flow only in another observation, resulting in the death of patient.

Key words: *coronary arteries, myocardial infarction, simultaneous thrombosis of the stent and second coronary artery.*

Abbreviations

OMB – obtuse marginal branch
CA – coronary artery
CG – coronarography
LV – left ventricle
CA – circumflex artery
LAD – left anterior descending artery
RCA – right coronary artery
ECS – Emergency Call Service
PCI – percutaneous coronary intervention
PIVB – posterior interventricular branch
PLA – posterior lateral artery
LV EF – left ventricular ejection fraction
CPK – creatinphosphokinase
HR – heart rate
EHA– electrical heart axis
EchoCG – echocardiography

Introduction

Cases of simultaneous thrombosis of two or even three coronary arteries (CA) have been described, but are rarely observed. Two variants are possible: development of simultaneous thrombosis in a few CA (1–10) and thrombosis of two CA in the area of earlier implanted stents (11–21). In both cases, this severe complication causes an extensive damage of the myocardium and requires immediate endovascular intervention in order to restore coronary blood flow. The risk of cardiogenic shock, lethal outcome and complications during CA interventions is higher for such lesion (12, 15).

In 2009–2011, simultaneous thrombosis of implanted stent and the second coronary artery within 3 to 8 days after the surgery occurred in two cases (0.09%) out of 2314 percutaneous coronary interventions (PCI) on the CA performed in our Institute. These complications required immediate repeated PCI. Both patients had multiple coronary lesions. These observations are provided below.

Clinical observations

Case 1. Patient E., female, 73 years old, was brought by the emergency care team with complaints of pressing pain behind the breastbone. Medical history: arterial hypertension (AH) for about 20 years with maximum elevation up to 220/110 mm Hg, impaired glucose tolerance. Occasional restrictive pain in the heart area has occurred for many years but was not clearly exercise-related. Condition has worsened three days before the admission, when suddenly a feeling of undulated "stabbing" retrosternal pain occurred, the pain intensity increased gradually. The patient presented to the polyclinics; the ECG signs of acute focal myocardial changes were detected. Morphine was administered at the pre-hospital stage to manage the pain.

At admission, her condition was severe. Blood pressure was 150/80 mm Hg. HR was 101 beats per minute. ECG revealed regular sinus rhythm. The

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Manuscript received on November 16, 2012
Accepted for publication on December 18, 2012

heart's electrical axis was in the horizontal plane. There were the signs of left ventricular myocardial hypertrophy. The following was observed: *QS* in V1–3, regression of *R* in V4–5, *ST* segment elevation in V1–3 up to 2 mm with initial signs of negative T formation in V2–3. Low negative *T* was detected in aVL.

EchoCG showed hypoakinesia of 4 apical segments, hypoakinesia of anterior and anteroseptal segments at the middle level (6 segments in total). LV ejection fraction was 44%. CPK – 1588 IU/L, CPK-MB – 103 IU/L, troponin – 3.60 ng/mL.

Coronarography (CG) performed 9 hours after the hospitalization revealed right type of coronary circulation; 60% stenosis of the left main coronary artery before the bifurcation; occlusion of the left anterior descending artery (LAD) in the proximal third with distal vessel filling via intrasystemic collaterals. Circumflex artery (CA): 60% stenosis was observed in the middle third, 70% stenosis in the 1st obtuse marginal branch (OMB), 90% stenosis in the 2nd OMB. Right coronary artery (RCA) was stenosed in the proximal third up to 60%, with diffuse lesions. Mechanical recanalization of the LAD using a guide wire and dilatation with a balloon catheter (diameter 2.25 mm, length 15 mm) was performed with subsequent implantation of bare metal "Liberte" stent (diameter 2.75 mm, length 16 mm, pressure 15 atm.). Residual stenosis was insignificant. No distal embolization was observed. There was no dissection. TIMI 3 blood flow was restored.

Post-intervention ECG showed: decrease of *ST* elevation in V2–3 up to 1.5 mm, persisting slow evolution of anterior myocardial infarction.

In 3 days, the patient suddenly developed intense restrictive chest pain, nausea and vomiting. ECG showed increase of *ST* elevation in V2–4 accompanied by *ST* depression in III, aVF up to 0.5 mm.

Repeated CG detected stent thrombosis in the LAD and in the 2nd OMB with 90% stenosis. The patient underwent mechanical recanalization, balloon dilatation of the stent in the LAD (balloon: 3 mm in diameter, 9 mm long; pressure 16 atm.) with subsequent mechanical recanalization using a guide wire and balloon angioplasty of the 2nd OMB (balloon catheter: 1.5 mm in diameter, 20 mm long; pressure 20 atm.). Residual stenosis was insignificant. No distal embolization was observed. TIMI 3 blood flow was restored in both arteries.

During EchoCG performed over time, the following was observed: regional contractility impairments (in the same 6 segments), the signs of left ventricular apical aneurism development (dyskinesia with thinning of anterior and septal apical segments up to 5–6 mm). LV EF was 43%. The patient was discharged in a fair condition.

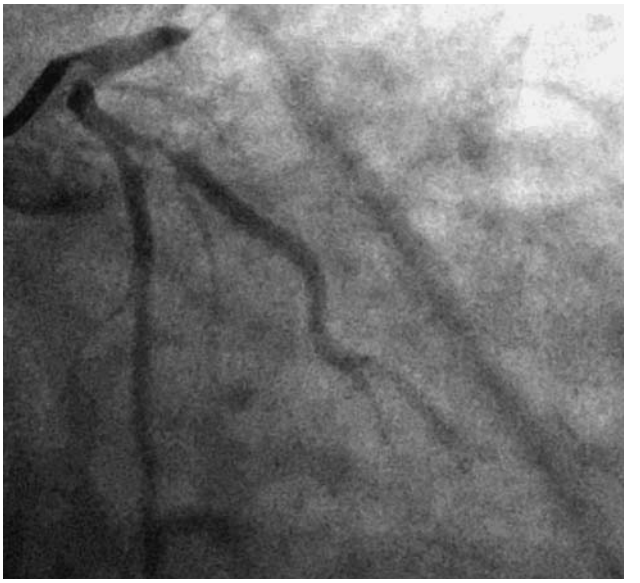

Figure 1. Occlusion in the proximal third of the left anterior descending artery (LAD), over 90% stenosis of the 1st obtuse marginal branch.

Case 2. Patient K., 67 years old, was brought to the Institute by emergency care team 3 hours after the onset of restrictive retrosternal pain, weakness and shortness of breath. The complaints of restrictive retrosternal pain on exertion, rapidly managed by nitroglycerin, first appeared about 2–3 weeks prior to hospitalization. At pre-hospital stage, pain syndrome was not entirely managed by intravenous morphine administration. At admission the patient's condition was extremely severe due to cardiogenic shock and pulmonary edema. Blood pressure at admission was 82/65 mm Hg. ECG data at admission were suggestive of transmural myocardial infarction of the anterior wall, septum, and apex of the left ventricle. EchoCG showed: dilatation of left atrium and left ventricle cavities; akinesia of 7 LV segments in the anterior wall, septum and apex; grade II mitral regurgitation, probably due to papillary muscle impairment. EF was 39%. Troponin – 10.79 ng/mL, CPK – 1144.65 IU/L, CPK-MB – 84.78 IU/L.

Diagnosis: acute transmural myocardial infarction of anterior wall, septum and apex of the left ventricle, involving the papillary muscle; atherosclerosis of aorta and coronary arteries, grade III arterial hypertension (according to the medical history).

In 25 minutes after hospitalization, the patient was brought to the catheterization laboratory. Balloon pump for intra-aortic counterpulsation was set in 1 : 1 mode. CG revealed: right coronary blood flow, unchanged left main coronary artery, LAD occlusion in the proximal segment, CA without stenosis, over 90% stenosis in the large 1st OMB (Figure 1); diffusely changed RCA, 50% stenosis in the proximal third, 90% stenosis in the middle third,

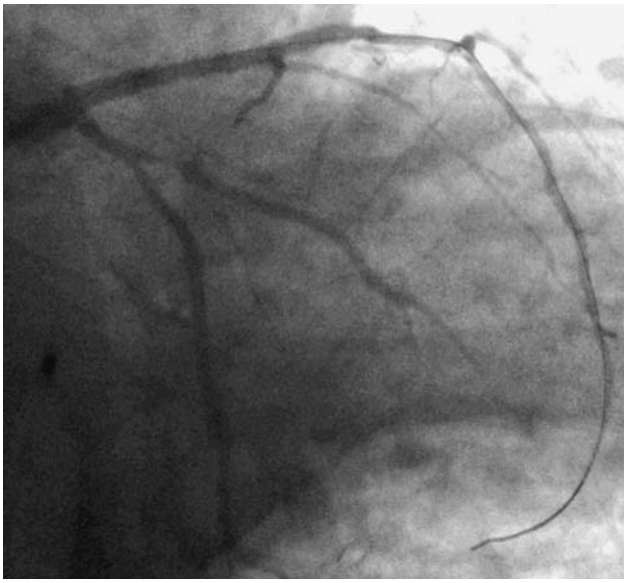

Figure 2. Coronary angiogram after blood flow restoration and LAD stenting.

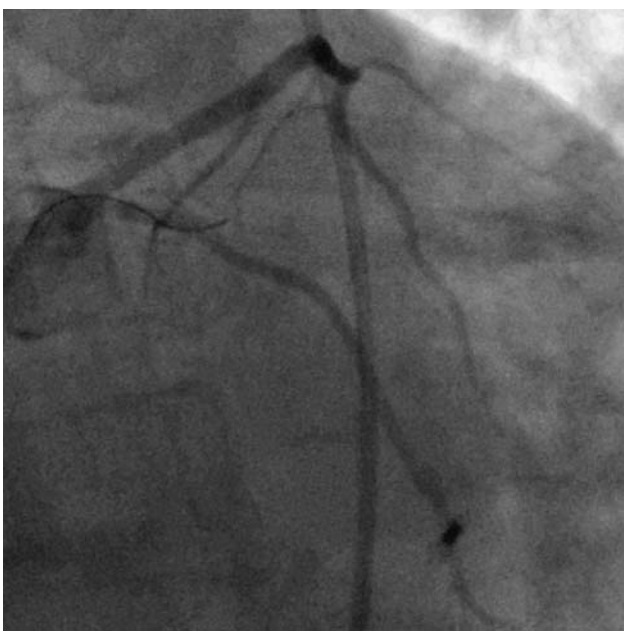

Figure 3. Coronary angiogram after repeated blood flow restoration in the LAD and attempted recanalization of the 1st OMB.

60–65% stenosis in the distal third, aneurysmatic dilatation in the bifurcation area, diffuse changes in the posterior descending artery (PDA) and in the posterior lateral artery (PLA). Mechanical recanalization was performed using a guide wire with subsequent balloon dilatation of the LAD (balloon catheter: diameter 2.75 mm, length 20 mm, pressure 16 atm.). Uncoated "Skylor" stent (diameter 3 mm, length 35 mm, pressure 20 atm.) was implanted. Additionally, balloon dilatation in the proximal part of the stent was performed using balloon 3.5 mm in diameter, 12 mm long (pressure 20 atm.). Residual stenosis was insignificant, no distal embolization was observed, TIMI 3 blood flow was restored (Figure 2).

In the postoperative period patient's condition remained severe. Manifestations of acute left ventricular failure decreased during the therapy; the signs of cardiogenic shock and pulmonary edema did not recur during dopamine infusion. Balloon pump for intra-aortic counterpulsation was removed on Day 4. Doses of cardiotonic support were gradually reduced until the complete withdrawal.

On day 8 angina attack recurred. ECG findings: atrial fibrillation, abrupt left electrical axis deviation, right bundle branch block, the picture of anteroseptal infarction. Cardiogenic shock developed.

Balloon pump for intra-aortic counterpulsation was re-inserted. CG revealed stent thrombosis in the LAD and thrombosis of the 1st OMB with > 90% stenosis. Mechanical recanalization of a thrombosed stent and balloon (3,5 × 20 mm) dilatation were performed. The lumen was completely restored (Figure 3). TIMI 3 blood flow was restored. Mechanical recanalization of an acute occlusion of the 1st OMB was attempted using different techniques; glycoprotein IIb/IIIa inhibitor, monofram, was administered. The attempt to restore blood flow in the OMB failed. Despite intensive therapy, the patient's condition progressively worsened and 3 days after the repeated intervention the patient died.

Discussion

There are few reports on simultaneous thrombosis of two or more coronary arteries; they describe single observations. Only Garbo et al. (3) have described 4 cases, and Maagh et al. (7) have had 5 observations. Kanei et al. (5), who in 2009 described a case of RCA and LDA thrombosis in a 37-year old patient, collected data on 23 similar observations in the literature. Mean age of patients was 53 ± 14 years (32–82 years old), 74% of them were males. The majority of patients had multiple risk factors of coronary artery lesions. LDA thrombosis was observed in 78% of cases, and RCA thrombosis – in 87%.

All these reports concerned simultaneous thrombosis of 2 coronary arteries. Turgeman et al. (10) presented a unique case when a 44-year old male had a myocardial infarction, cardiogenic shock; besides, during the coronarography LAD and RCA thrombosis, as well as a mobile thrombus in the CA were detected.

Rare cases of simultaneous thrombosis of two implanted stents in different coronary arteries have also been described (11–21). Frynas et al. (13) provide data stating that thrombosis occurs in 0.5–1.9% of cases when using uncoated stents, and they describe a case of simultaneous thrombosis of two

uncoated stents 3 days after their implantation into different coronary arteries.

Other reports describe single cases of simultaneous thrombosis of two drug-eluting stents (11, 12, 14–20); van Werkum et al. (21) provided 3 such observations. Thrombosis may develop in any time period after implantation: in 8 hours (14), 4 days (12), 7 days (17), 2 years (20), 3 years (18). Discontinuation of antiaggregant therapy, e.g. prior to the surgery, may result in thrombosis (15, 18, 19).

The mechanism of simultaneous thrombosis of two coronary arteries at once or two stents implanted in different arteries is not entirely clear (2). In Turgeman et al. opinion (10), the plaque rupture in some patients with cardiogenic shock, resulting in acute thrombosis of one coronary artery, may lead to low coronary pressure and gradual thrombus formation in another artery. Bartel et al. (1) believe that simultaneous tear of two plaques with thrombosis is possible in rare cases of extensive coronary lesions.

In van Werkum et al. opinion (21), although the search for triggering mechanism of simultaneous thrombosis of two stents still remains purely speculative, it may be affected by suboptimal stent size with, perhaps, underexpansion and thrombosis, coagulation system activation, impaired hemodynamics and thrombosis of the second stent. However, these suggestions are unlikely suitable for thromboses occurring in 2 or 3 years (18, 20). Impaired blood coagulation system, diabetes mellitus, the level of C-reactive protein and other factors may affect the simultaneous thrombosis (1, 11).

In case of simultaneous blood flow cessation in two coronary arteries, the patient's condition is severe, which requires immediate intensive care, resuscitation measures, the use of intraaortic balloon pump counterpulsation, coronary blood flow restoration using X-ray endovascular techniques.

Luminal restoration was achieved by means of aspiration thrombectomy (5, 10), complemented by administration of glycoprotein IIb/IIIa inhibitors (8) and implantation of stents (2). Mechanical recanalization, balloon dilatation and stenting (6) were performed; abciximab was additionally administered for myocardial perfusion improvement (1). Hosokawa et al. (4) performed angioplasty of one artery and intracoronary thrombolysis (6,400,000 IU of tisokinase) in another artery. Mechanical recanalization using a guide wire and balloon angioplasty is most commonly used in case of two stent thrombosis (12, 13). Moon et al. (16) administered ReoPro and conducted thrombi aspiration with subsequent administration of aspirin + clopidogrel + cilostazol to prevent thrombosis of two drug-eluting stents.

Stent thrombosis combined with the 1st OMB (in one case) and the 2nd OMB (in the second observation) thrombosis with 90% stenosis occurred in the provided observations. Mechanical recanalization and balloon dilatation of the stent and the 2nd OMB were performed in the first patient; the patient was discharged in a fair condition. In the second patient, we were able to restore only the blood flow in the stent. The patient's condition was initially severe due to cardiogenic shock. Although the blood flow in the LDA stent was restored during the second intervention, severity of condition at baseline and the extent of myocardial damage still led to the lethal outcome in 3 days.

Conclusion

Simultaneous thrombosis of two coronary arteries and stents in different variations is a rare severe condition, fraught with cardiogenic shock and lethal outcome. Optimal treatment tactics is an urgent coronary blood flow restoration using various endovascular techniques.

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Staged Endovascular and Surgical Intervention on Carotid, Renal and Coronary Arteries in a Female Patient with Takayasu Syndrome (a Clinical Case)

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Stenotic occlusive lesion of the renal arteries causes 2–3% of all cases of arterial hypertension (1, 2). In 70–80% of patients, kidney circulation disorders are caused by stenotic atherosclerotic process, in 15–20% – by fibromuscular dysplasia, and in 5–10% of cases – by aortoarteritis, including Takayasu syndrome characterized by the development of productive inflammation in artery walls mainly of large arteries, resulting in their obliteration (1, 3). Thus, progressive course of the disease within 3 years results in complete occlusion of impaired arteries (including renal ones) in 15–20% of patients (4, 5). Clinically, renal artery occlusion manifests in renovascular hypertension (33–83%), progressing of renal failure and an increased risk of cardiovascular events (6). The use of interventional treatment methods for narrowing of renal arteries, generally, made it possible to achieve favorable clinical results with a low incidence of complications at the in-hospital stage (7, 8). Young women, as a rule without atherosclerotic lesion of the coronary vessels, prevail among the patients with Takayasu syndrome. Meanwhile, an accelerated development of atherosclerosis in a lingering course of the disease, which may be related both to an inflammatory activity and the conducted treatment with glucocorticoids and cytostatics, is currently under discussion. Thus, coronary arteries are involved in the pathological process in 3–10% of patients, and angina symptoms are observed in 14% of patients (10). Meanwhile, the preferable method of coronary heart disease (CHD) treatment in these patients, as well as the efficacy and appropriateness of blood flow restoration in a continuously "chronically" occluded renal artery, remains disputable. On the other hand, in the emergency situations caused by spontaneous or iatrogenic occlusion of the renal artery, blood flow restoration is a necessary measure to prevent renal infarction and renal failure (9).

The results of stenting of the continuously occluded renal artery and coronary bypass surgery, conducted in a female patient with Takayasu syndrome, have been reviewed in this clinical case. 52-year old female patient G. was admitted to the clinic on December 21, 2009 diagnosed with CHD; functional class (FC) III effort angina; multifocal atherosclerosis, Takayasu syndrome; occlusion of the right common carotid artery (CCA), internal carotid artery (ICA), external carotid artery (ECA); a condition after resection of the right ICA, endarterectomy of the right CCA and ECA, autoarterial reconstruction of the right ECA dated December 12, 2008; thrombosis of the right ECA; a condition after endarterectomy of the left CCA, ICA and ECA. It is known from the medical history that the patient has suffered from the arterial hypertension for 10 years, with blood pressure (BP) increasing up to 260/140 mm Hg during the past 6 months; the patient is adapted to blood pressure of 160/100 mm Hg and regularly has been taking Renipril to decrease the pressure (20 mg/day). Angina attacks started about 2 years ago, occurring during the moderate physical activity; for the last year, painless walking distance has reduced from 500 to 200 meters. Occlusion of the right internal carotid artery and 70% stenosis of the left internal carotid artery for the first time were revealed in April 2008 during the ultrasound dopplerography (USDG). Resection of the internal carotid artery, endarterectomy of the right CCA and ECA, autoarterial reconstruction of the right ECA were performed at the City Clinical Hospital No. 57 in December 2008. At that time, based on the clinical data, she was diagnosed with Takayasu syndrome for the first time. In May

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Manuscript received on October 3, 2012.
Accepted for publication on December 19, 2012.

2009, at that place, carotid endarterectomy of the left CCA, ICA and ECA was performed using a shunt. Taking into account progressing of the angina, diagnostic coronary angiography (CAG) was performed in June 2009 at the City Clinical Hospital No. 57, which revealed the following multivessel stenotic lesions of the coronary arteries: stenosis of the middle third of the left anterior descending artery (LAD) up to 70%; 75% stenosis of the proximal third of the left circumflex artery (LCX); 80% stenosis of the obtuse marginal branch (OMB) orifice, as well as stenosis of the distal third of the right coronary artery (RCA) up to 80%. According to CAG data, the patient was recommended to undergo direct myocardial revascularization, but at that time she abstained from the procedure. Since August 2009, a dragging pain in the left lumbar region has appeared. In October 2009, according to the results of conducted computed tomography, an occlusion was revealed at the site of the surgical intervention on the right CCA, ECA and ICA, as well as occlusion of the left renal artery, atrophy of the upper and middle segments of the left kidney (arteriosclerotic left kidney); at that time, increased levels of urea and creatinine were registered in the blood chemistry for the first time. Of concurrent diseases, the patient reports diabetes mellitus for 5 years, for the treatment of which she has been taking Diabeton MV (30 mg/day). In 1997, she underwent the removal of the left adrenal gland due to a 24 × 20 mm mass. For correction of adrenal insufficiency, the patient has been continuously taking prednisolone (7.5 mg/day), cortinef (0.2 mg/day). For the past 3 months she has been receiving the following drug therapy: Renipril at a dose of 10 mg twice a day; Vasocordin 25 mg/day, Cardiket 40 mg/day, Vasilip 20 mg/day, Mexicor 100 mg/day. Taking into consideration coronary history, as well as renal dysfunction, she was hospitalized to the Center of Cardioangiology in December 2009 for repeated coronary angiography, angiography of the renal arteries and for determination of the further treatment tactics. On admission: the condition was fair; the skin and mucous were of normal color and moisture level. Vesicular breath sounds were heard on auscultation, no rales were noted. The heart borders were displaced to the left (+1 cm). Tones were muffled, rhythmic, no murmurs were auscultated. The heart rate was 68 beats per minute, arterial pressure on the left hand was 170/100 mm Hg; no pressure was detected on the right hand. Pulsation on the peripheral arteries of the legs was abruptly decreased. Digestive system was unremarkable. Urinary system: urination was not impaired, Pasternatsky's symptom was negative on the both sides. Neurological status was unremarkable. During the conduction of laboratory studies, a lot of squamous epithelium in the urine analysis and increased levels of urea up to 11.3 mmol/L and creatinine up to 101 μmol/L were of note, as well as the increase of C-reactive protein up to 13.5 mg/L. According to the data of instrumental investigation methods, the following was observed on ECG: regular sinus rhythm. Heart rate was 66 beats per minute; deviation of the heart's electrical axis and *QS* wave in the 3rd avF lead was observed. Smoothed T waves in V4–V6 leads were registered. There were no negative changes as compared with anamnestic ECG. On Echo-CG: cardiac cavities were not enlarged, valves were unremarkable; left ventricle (LV) ejection fraction (EF) was 67%, contractility was satisfactory, no asynergy zones were revealed. Additionally, a chord was located in the left ventricular cavity along the interventricular septum; aorta was thickened, not dilated. According to 24-hour ECG monitoring: no rhythm and contractility disorders were revealed. 1.5 mm *ST* segment depression was observed at the first channel, mostly related to the physical exertion and pain.

The patient underwent diagnostic CAG and angiography of the renal arteries: the right type of the coronary blood flow was detected, the left main coronary artery was developed as usual, without changes. LAD was diffusely impaired with extended 75% stenosis in the middle third. LCX had 70% stenosis in the proximal third and 75% stenosis in the middle third. The 1st marginal branch, about 2 mm in diameter, was stenosed by 70%; RCA was moderately diffusely impaired in all departments with over 80% stenosis in the distal segment. Lesion severity score was 14 according to Syntax scale. According to the data of renal aorto-arteriography, an ostium stenosis of the right renal artery up to 30% was observed, the left renal artery was occluded from the orifice (Figure 1A, B).

A successful mechanical recanalization and angioplasty of the left renal artery were performed via the right transfemoral approach. RDC I Cordis 7F renal guide catheter was placed into the stump of the left renal artery (Figure 2, A). Recanalization was conducted via Shinobi hydrophilic coronary guide wire. Then, predilatation with small diameter Maverick Boston Scientific coronary balloon (1.5 × 20 mm) was performed (Figure 2, B).

After test injections of the contrast medium and after confirming that a distal end of the guide wire was placed in the lumen of the occluded renal artery, a consecutive dilation via various balloon catheters with maximal diameter of 5.0 mm was performed. (Ultra thin Diamond Boston Scientific, 5,0 × 20 mm).

Considering the presence of over 40% residual stenosis after balloon dilation (Figure 3 A, B) and in order to improve a long-term prognosis of the endovascular procedure, it was decided to implant

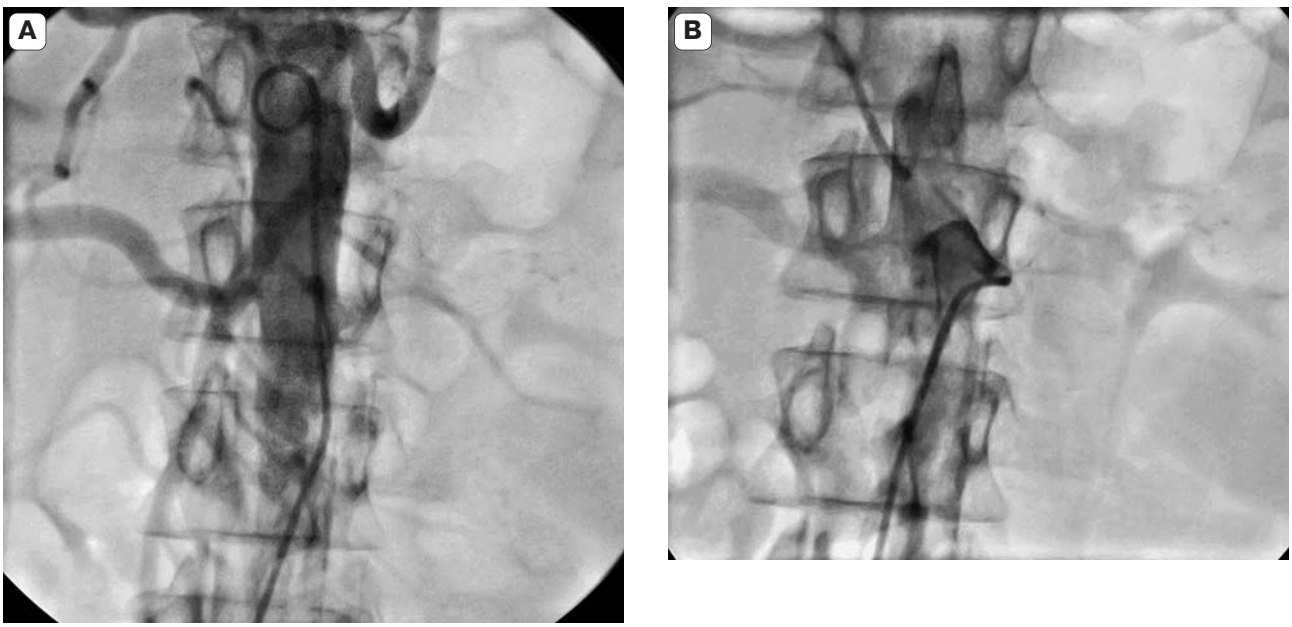

Figure 1. Angiography of the renal arteries in a patient G., 52 years old: A – abdominal aortography; B – selective angiography of the left renal artery.

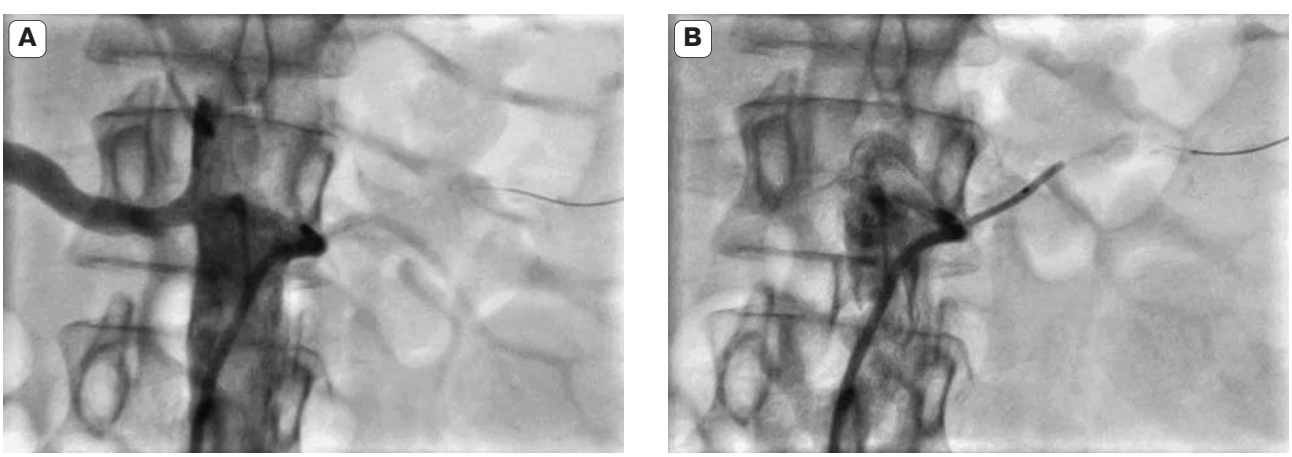

Figure 2. Mechanical recanalization (A) and balloon dilatation (B) of the left renal artery.

5.0 × 28 mm Eucatech AG balloon-expandable stent. A peripheral stent was placed with a good angiographic result (Figure 4). Normalization of BP to 120/80 mm Hg was clinically observed in a patient during the intake of decreased daily dose of calcium antagonists. On Day 3 after the interventional procedure, control ultrasound examination of the left renal artery was performed: good magistral blood flow was observed in the left renal artery with no signs of stenosis.

Blood chemistry also confirmed a positive result of conducted endovascular procedure, which manifested as a decrease in the level of urea from 11.9 till 6.1 mmol/L and creatinine from 100 μmol/L to 87 μmol/L.

The patient was discharged for the follow-up at her place of residence with recommendations to take Plavix at a dose of 75 mg/day, Normodipine (5 mg/day), Diclofenac (100 mg/day), and recommendations on repeated hospitalization to the inpatient department for a complete myocardial revascularization (CABG). On June 15, 2010, mammary coronary bypass grafting (MCBG) of the LAD, autoarterial CABG of the 2nd marginal branch (MB) and autovenous CABG of the 1st marginal branch (MB) and the RCA were conducted. In the early postoperative period, manifestations of relative renal failure were observed that resolved after detoxification therapy. The patient was discharged for aftertreatment in Bykovo suburban rehabilitation department. The patient's condition improved, which increased in the improved physical tolerance. The blood levels of creatinine and urea were normal (93 mmol/L and 4.8 mmol/L, respectively).

The patient underwent a control examination in December 2010. No evidence for inflammation was obtained from the laboratory tests. During multispiral computed tomography (MSCT) of the coronary

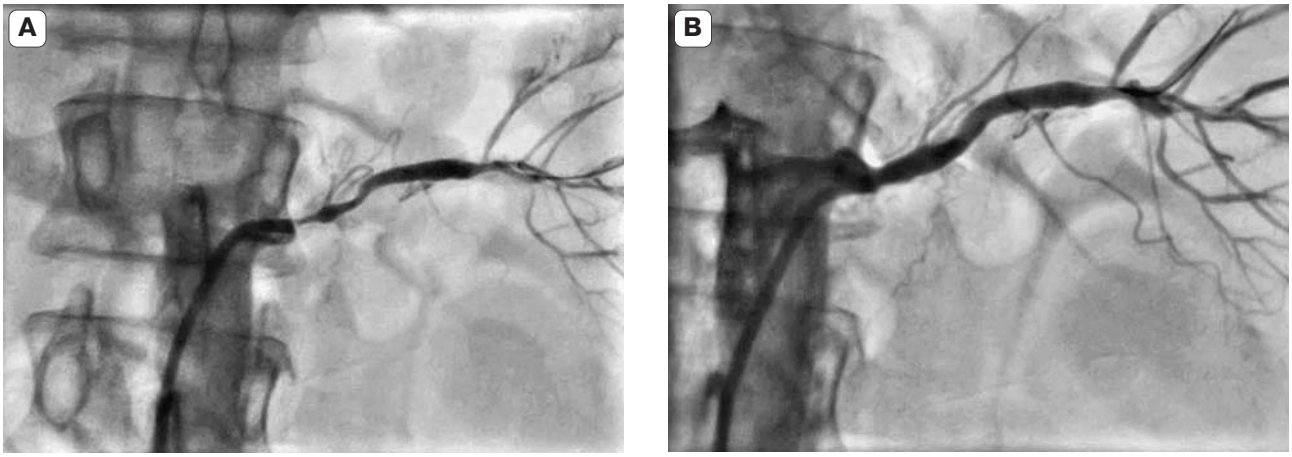

Figure 3. Immediate results of dilation via 3.0 mm balloons – (A) and 5.0 mm balloons – (B) of the left renal artery in a patient G., 52 years old.

Figure 4. Implantation of 5.0 × 28 mm Eucatech AG balloon-expandable stent. Immediate result of mechanical recanalization and stenting of the left renal artery in a patient G., 52 years old.

Figure 5. In-stent stenosis of the left renal artery.

and renal arteries, a good condition of the shunts to the coronary arteries and the signs of stent restenosis were observed along the whole length of the left renal artery. MSCT data coincided with the results of diagnostic coronarography, shuntography and angiography of the left renal artery. During the coronarography, atherosclerosis progression was observed in the native arteries: the left main coronary artery was developed as usual, without changes. LDA was occluded in the middle segment. LCX had 90% stenosis in the proximal segment and was occluded in the middle segment. RCA was occluded in the distal segment. Shunt in the left internal thoracic artery (ITA) to the LAD, as well as A-A shunt to the obtuse marginal branch (OMB2) and AV-shunt to the obtuse marginal branch (OMB1) and the RCA were not impaired and functioned normally. Angiography of the brachiocephalic artery (BCA): Right CCA was occluded from the orifice. Left CCA, ICA and ECA had no zones of hemodynamically significant stenosis. According to the angiography of the left renal artery, in-stent stenosis of the left renal artery was detected (Figure 5).

Single-stage balloon angioplasty of in-stent stenosis of the left renal artery using 5.5 × 20 mm Ultra-soft Boston Scientific balloon catheter was performed with good immediate angiographic and clinical result (Figure 6).

On Day 5, the patient was discharged from the inpatient department in a fair condition (with her regular arterial pressure).

Overall, this clinical case demonstrates the rapid progression of coronary atherosclerosis in a female patient with Takayasu syndrome and type 2 diabetes mellitus, whose coronary shunts were in a good state, as well as a tendency to restenosis during percutaneous coronary intervention (PCI) using standard bare metal stents (BMS). And this coincided with a general outlook on this problem. As demonstrated by the medical practice worldwide, percuta-

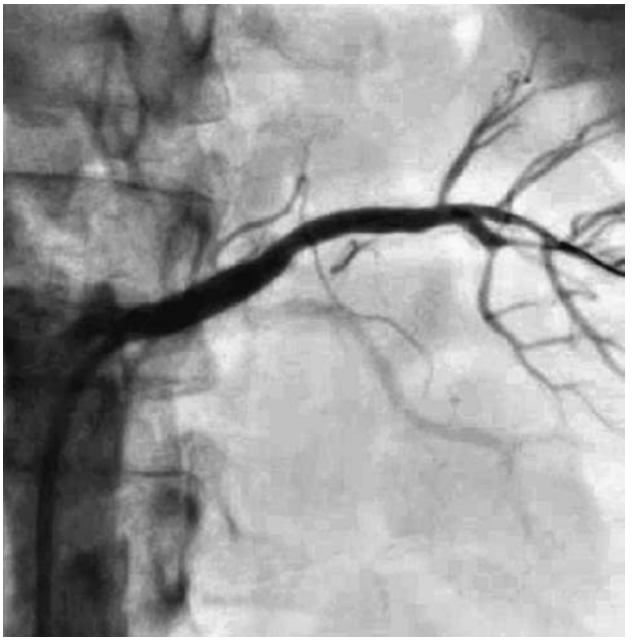

Figure 6. Balloon angioplasty of the in-stent stenosis of the left renal artery.

neous coronary angioplasty in a substantial number of patients with Takayasu syndrome is accompanied by restenosis in 1–2 years; coronary artery bypass surgery is characterized by more preferred long-term results.

In conclusion, this clinical case illustrates the appropriateness and efficacy of staged endovascular treatment of the renal arteries and direct myocardial revascularization in patients with Takayasu syndrome in remission. Unsatisfactory angiographic results of stenting using bare metallic stents in this group of patients require the use of drug-eluting stents. Meanwhile, we should emphasize, that it is of singular importance to correct the classic risk factors for cardiovascular diseases such as dyslipidemia, hypertension, bad habits, as well as the importance of an obligatory intake of aspirin at low doses.

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Stent Thrombosis and Coronary Artery Aneurysm after Implantation of a Sirolimus-Eluting stent (Cypher) and Two Standard Bare Metal Stents (Bx Sonic) in the Same Patient (Clinical case)

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The use of drug-eluting stents for the treatment of stenotic coronary artery lesions demonstrated their benefits as compared with bare metal stents (BMS) both in decreasing the rate of restenoses to 3% and in reducing major adverse cardiac events (MACE) during the immediate and mid-term period after the endovascular procedure (EVP). However, the problem of late stent thrombosis (0.6% per year), associated with severe complications and fatal outcomes, was revealed while studying the long-term results of the drug-eluting stents (DES) usage. Preliminary conclusions were made based on the conducted studies: 1) stent thrombosis (*ST*) occurs both after BMS and drug-eluting stent implantation; 2) there are almost no differences in the overall incidence of *ST* between eluted and bare stents in the mid-term period; however, there are data on more frequent late occurrence of *ST* following the implantation of drug-eluting stents as compared with BMS; 3) along with premature termination of double antiaggregant therapy (acetylsalicylic acid + clopidogrel), development of local coronary artery aneurysms may be one of the causes of late DES thrombosis as opposed to BMS (1–3; 9–12).

Implantation of DES as opposed to BMS activates cascade of time-expanded stages of healing, consisting of 5 separate processes: 1) thrombotic stage (sedimentation of platelets – it may last up to 14 days, and fibrin accumulation – up to 30 days); 2) inflammatory stage (it starts immediately after stent implantation and lasts for at least 3 months); 3) the stage of tissue granulation (proliferation of smooth muscle cells in combination with chronic cellular infiltration); 4) development of the extracellular matrix, which components (proteoglycans and collagen subtypes) serve as the basis for the developing restenotic structure – it can last for over a year; 5) vascular wall remodeling stage – it can last for more than 18 months. (4–6). Damage of the arterial wall caused by a drug-eluting stent results in delayed healing, which may be related to a delayed type hypersensitivity allergic reaction (5–7). DES successfully inhibits proliferation of smooth muscle cells, thus reducing the possibility of restenosis; however, it promotes prolongation of fibrin accumulation stage, thus increasing the possibility of thrombosis. Simultaneous prolongation of inflammatory response (over 90 days) and deceleration of endothelization process are observed. Nebecker et al. (7), as well as Virmani et al. (8) consider that stent-related hypersensitivity is likely to occur as a response to a synthetic polymer, included in their composition, which is not soluble and is a source of chronic aseptic inflammation. This is indirectly confirmed by the following intravascular ultrasound (IVUS) data: accumulation of eosinophils, giant cells and white blood cells at the site of DES implantation. This, in turn, results in a deep destructive effect of coated stents on the vascular wall, with its thinning and possible formation of local vascular aneurysms in the remote period, which is also a significant risk factor for the development of *ST* and cardiac complications (9–11).

Thus, the uncertainty and the lack of unanimous approach to the problem of late *ST* and coronary aneurysms when using DES are mainly explained by the delayed aneurysm formation and the low incidence of these complications. Comparative assessment of bare metal stents and drug-eluting stents was performed in the separate patient groups. We have a clinical case, when both types of stents were implanted to the same patient, which guaran-

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Manuscript received on October 17, 2012.
Accepted for publication on December 19, 2012.

teed equal autoimmune response to the implantation of stents. In terms of solving this problem, we are interested in discussing the long-term angiographic results in a patient with implanted DES (Cypher) and BMS (Bx Sonic) and receiving long-term maintenance double desaggregant therapy (acetylsalicylic acid and clopidogrel).

Clinical case

Patient B., 54 years old, was hospitalized via the ambulance team to the Resuscitation and Intensive Care Unit (RICU) at the Scientific and Practical Centre of Interventional Cardioangiology on March 31, 2005 due to developed angina attack and revealed acute focal myocardial changes on ECG. Diagnosis on admission: CHD; Acute non-Q-wave posterior diaphragmatic myocardial infarction (>6 hours from the onset of angina attack).

No blood pressure (BP) elevations were observed according to the medical history. The patient tolerated physical exertions well, without experiencing any chest pain. The patient was a smoker, without a history of alcohol abuse. There were CHD hereditary problems (through the male line). Condition suddenly worsened on the day of admission; pressing pain behind the breastbone occurred during psychoemotional exertion, lasted about 1 hour and was accompanied by numbness of both hands, sweating. The pain was managed after I/V administration of non-narcotic analgesics.

On admission to the in-patient department (>6 hours from the onset of angina attack), the patient reported no chest pain. Condition on admission was moderate. Skin was of normal color and moisture level. Harsh breath sounds could be heard over all parts of the lungs on auscultation, no rales were noted. Heart tones were moderately muffled, rhythmic. HR was 65 bpm. BP was 145/65 mm Hg. The abdomen was soft on palpation, painless in all areas. The liver edge was at the rib margin, painless on palpation. No edema was observed.

ECG on admission showed: regular sinus rhythm. PQ 0.12 seconds. QRS 0.09 seconds. *ST* segment elevation up to 1 mm in aVF lead, reciprocal depression of *ST* segment to 1 mm in aVL lead. Blood test showed: elevation of CPK-MB fraction, moderate leukocytosis, positive myoglobin test, positive troponin test, as well as dislipidemy, type IIb: total cholesterol – 6.4 mmol/L, triglycerides – 2.28 mmol/L.

Taking into account the time from the MI onset and the absence of angina, coronary angiography (CAG) for urgent indications was not conducted. Further, angina pain did not recur and hemodynamic parameters remained stable with conducted conservative treatment. Echo-CG showed: moderate hypokinesia of posterior wall of the LV in the basal third, overall contractility was satisfactory, LV EF = 58%, Grade I mitral regurgitation. Stress test was performed on Day 10 from the disease onset; it was accompanied by discomfort in the chest and changes on ECG such as *ST* segment depression by 1 mm in V5–6, exercise tolerance was high.

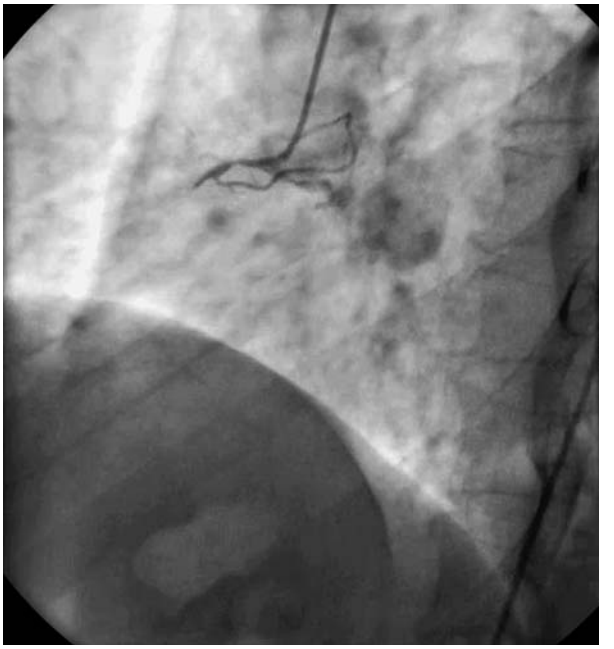

Figure 1. Chronic RCA occlusion in the proximal segment.

Diagnostic coronary angiography and ventriculography (VG) were conducted on Day 11 of acute myocardial infarction (AMI) in order to determine the state of the coronary vessels and to make a decision on further treatment tactics. The following was detected: moderate hypokinesis of inferior-basal segment, LV ejection fraction was 55%. The type of coronary blood flow was balanced. Left anterior descending artery (LAD) and left circumflex coronary artery (LCX LCA) were without changes. Right coronary artery (RCA) was occluded in the proximal segment; its distal segment was adequately filling through the intersystem collaterals. (Figure 1)

Given the examination data (VG and CAG, the results of stress test and the clinical course of the disease), the patient was recommended to continue conservative treatment with desaggregants (aspirin), a small dose of ACE inhibitors, nitrates, β-blockers and statins, to keep a diet, control lipids and quit smoking.

In May 2005, in view of ineffective antianginal therapy and recurrence of angina attacks, the patient underwent the following endovascular procedures **at Miasnikov Research Institute of Clinical Cardiology of Russian Cardiological Scientific and Production Complex:** mechanical recanalization, transluminal angioplasty and stenting

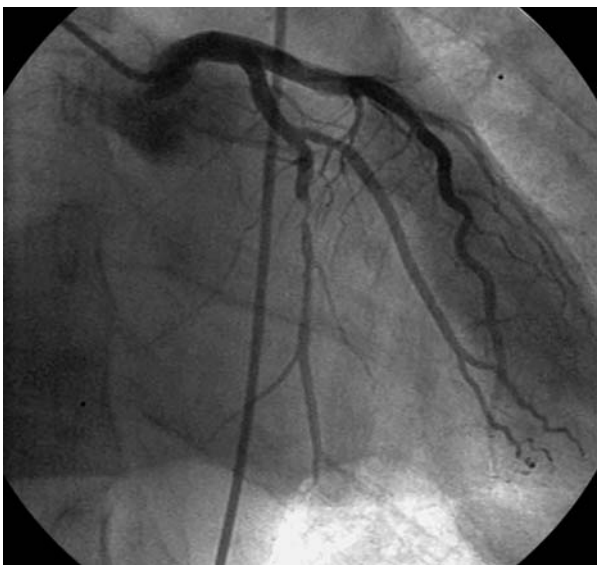

Figure 2. Stenotic lesion in the middle third of the LCX LCA.

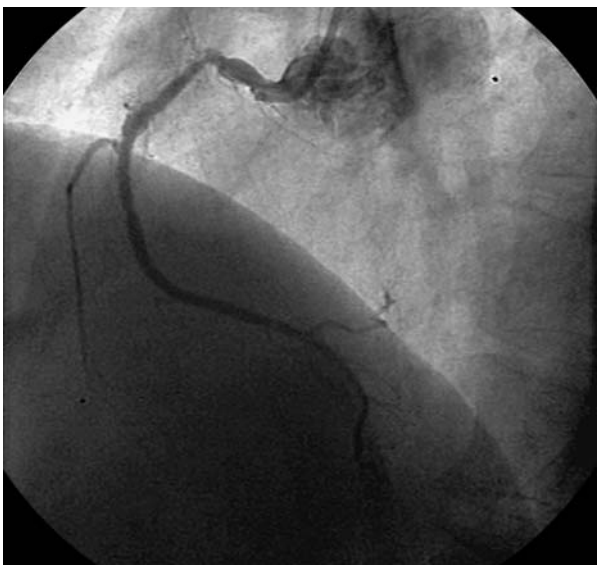

Figure 3. In-stent stenosis at the proximal end of the RCA stent.

Figure 4. Immediate result of the stenting in the middle third of the LCX LCA.

Figure 5. Immediate result of BMS endografting of the proximal third of the RCA, local aneurysmatic dilation at the distal part of the stent.

of RCA proximal segment using a drug-eluting stent (Cypher 2.75 × 33). After discharge, a long-term intake of aspirin, clopidogrel, beta-adrenoblockers and statins was recommended for a patient. The patient's condition remained stable with conducted therapy, angina pain was no bothering him, he tolerated physical exercises well; lipid profile was as follows: total cholesterol – 5.0 mmol/L, triglycerides – 1.64 mmol/L, LDL cholesterol – 2.8 mmol/L, CRP –0.

On November 19, 2006, the patient was again admitted to the Scientific and Practical Center of Interventional Cardioangiology with repeated myocardial infarction (in the area of scarring). Emergency CAG and VG showed: hypokinesia of diaphragmatic and inferior-basal segments with a decreased overall contractility (LV EF = 49%); progression of atherosclerosis, manifesting as abrupt (>70%) stenosis in the middle segment of the LCX LCA (Figure 2), and in-stent stenosis at the proximal end of the RCA stent and aneurysmal local dilation of this artery at the distal end of the stent (Figure 3).

Direct stenting procedure was performed in the middle third of the LCX (Bx Sonic 3 × 13), as well as transluminal angioplasty and stenting of the RCA (Bx Sonic 3.5 × 8 at the proximal part of the native artery in front of the previously implanted DES) with good immediate angiographic result. (Figure 4, 5).

Rare angina attacks persisted in the patient with moderate physical activities after discharge for the following 1.5 years during the intake of statins, calcium antagonists and antiaggregant therapy (aspirin). The patient voluntarily discontinued aspirin + clopidogrel 6 months after his last discharge.

On July 18, 2007, the patient was re-admitted to the Scientific and Practical Center of Interventional Cardioangiology with unstable angina.

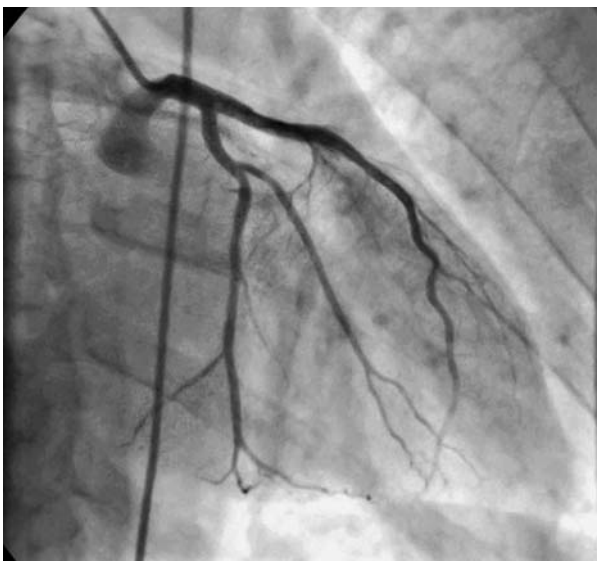

Figure 6. Good long-term (8 months) result of the LCX LCA stenting.

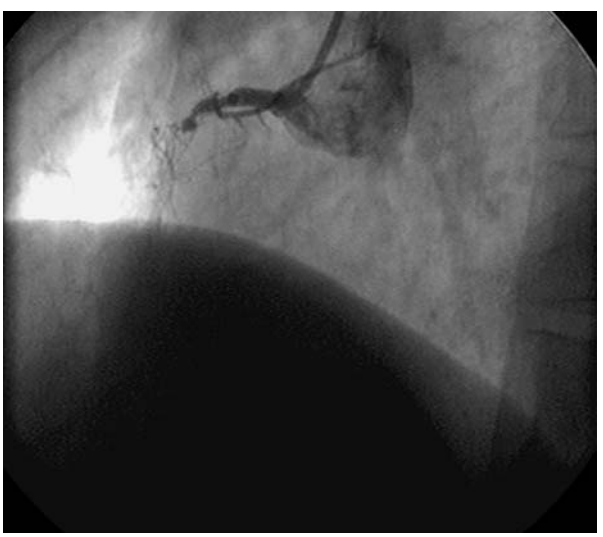

Figure 7. Occlusion of the stent at the proximal segment of the RCA.

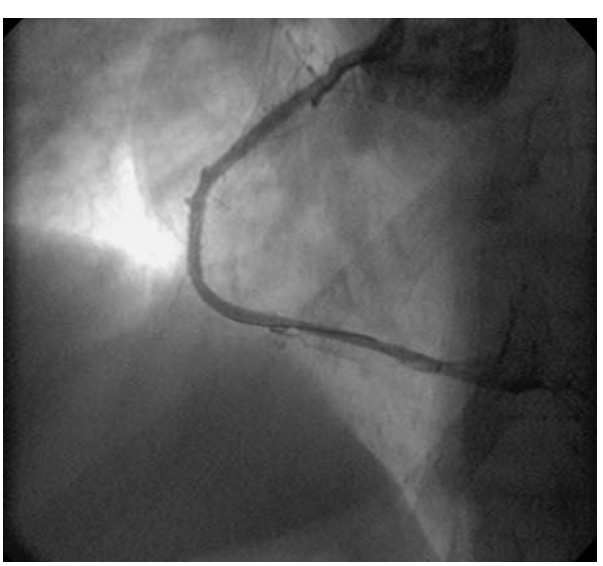

Figure 8. Immediate result of mechanical recanalization and angioplasty of the RCA.

After his condition stabilized, he was transferred to the cardiology department. No data on myocardial damage were obtained according to the blood test; total cholesterol and triglycerides did not exceed acceptable limits. Myocardial ischemia (*ST* segment depression to 2 mm in V5–V6 leads), accompanied by angina pain, was observed during the stress test. Follow-up VG and CAG were conducted on July 24, 2007 and the following was detected: moderate hypokinesis of diaphragmatic and inferior-basal segments, LV ejection fraction was 58%; earlier stented middle segment of the LCX LCA without the signs of restenosis (Figure 6); in RCA proximal segment, main stent occlusion (probably, at the site where BMS distal and DES proximal ends "overlap") (Figure 7). Mechanical recanalization and transluminal angioplasty of the RCA were conducted at the different levels with good angiographic effect (Figure 8).

Later on, the patient continuously received statins, ACE inhibitors and β-blockers, desaggregants (aspirin + clopidogrel). Condition was fair without angina attacks; physical activity was well tolerated.

The patient was repeatedly electively hospitalized at the Scientific and Practical Center of Interventional Cardiology on **July 24, 2009** due to occurrence of angina sings with insignificant physical exertions. On examination: myocardial contractility was satisfactory, moderate hypokinesis of the basal third of the posterior wall was observed; left ventricular ejection fraction was 62%. Stress test was positive: *ST* segment depression by 1 mm in leads II, III, aVF, V4–V6, angina pain. Blood test showed: CRP – 0, hypercholesterolemia – 6.6 mmol/L. On follow-up CAG: a long-term result of stenting in the middle third of the LCX was preserved; in-stent stenosis was detected in the body and at the distal end of the "coated" stent in the RCA; aneurysmatic dilation at the distal end of the DES increased in size (Figure 9). Transluminal angioplasty of in-stent stenosis was performed with good angiographic effect (Figure 10).

The patient was discharged in a fair condition with recommendations to continue intake of statins (with increasing the dose of the drug up till the adequate one) and double desaggregant therapy.

Discussion

The clinical case, provided above, clearly demonstrates the unsatisfactory long-term angiographic result and the need for repeated revascularizations after DES implantation in some patients, while a good long-term result is observed in the same patients when using BMS. In some authors' opinions, local vascular aneurysm is formed at the site of DES implantation due to a chronic inflammatory process that

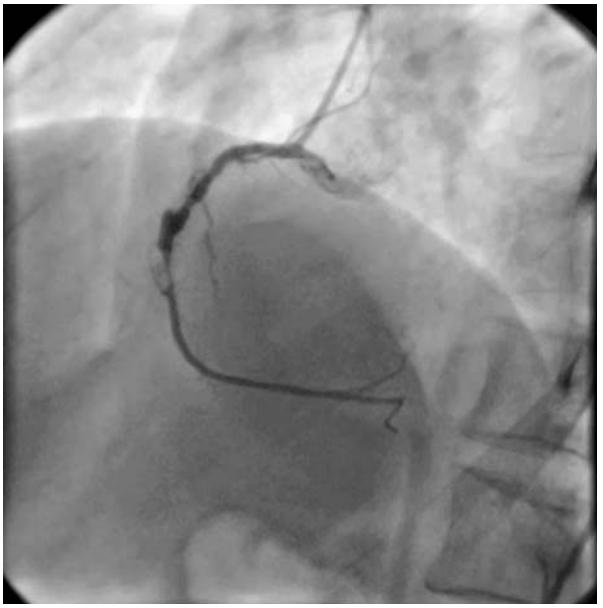

Figure 9. In-stent stenosis at the proximal and middle segments of the RCA. Local aneurysmatic dilatation at the distal end of DES.

Figure 10. Good result of restenosis angioplasty in the RCA stents. Local aneurysmatic dilatation at the distal end of DES is still present.

results in the thinning of the arterial wall. As compared with implanted BMS, DES polymer coating was likely to be that “irritative agent” which caused chronic aseptic inflammation (9–11). Luthra et al. (9) have demonstrated that chronic inflammation at the implantation site may cause thinning, erosion and lead to formation of aneurysmal dilatation of the vascular wall while on long-term double antiaggregant therapy. Övünç et al. (12) also described a case of coronary artery aneurysms formation 1 year after implantation of sirolimus-eluting stents.

In the process of solving this problem, recent efforts to reduce the risk of *ST* have been focused on the development of polymers with higher biocompatibility or biodegradability in order to release the drug; clinical trials of new stent platforms produced from polymers with decreased surface area (tanks) are ongoing as well. Other strategic approaches are aimed at improving engraftment by adding antithrombotic agents into the polymer coating, by completely withdrawing from the use of metal alloys and by starting to use biodegradable stent platforms (scaffold).

Thus far, there are unsolved issues on how to increase DES safety. A rigorous selection of patients for implantation of "coated” stents, as well as an early detection of patients with hypersensitivity to DES polymer in order to define indications for prescribing long-term double desaggregant therapy (aspirin and clopidogrel) exactly in such patients may be one of the ways to prevent development of coronary artery aneurysms associated with DES implantation and DES late thrombosis.

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Protection from Distal Embolization in Infarct-Related Artery during Endovascular Interventions in Patients with Acute Myocardial Infarction: State-of-the-Art and Perspectives

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Abbreviations

ACC/AHA – American College of Cardiology/ American Heart Association
MBG – Myocardial blush grade
TIMI – Thrombolysis In Myocardial Infarction
TBS – Thrombus burden score
IRA – infarct-related artery
AMI – acute myocardial infarction
EVI – endovascular intervention
DE – distal embolization

Currently, it can be considered to be proved that the earliest and most complete blood flow restoration in the infarct-related artery (IRA) improves the clinical prognosis in AMI patients, reduces mortality and incidence of serious complications (1, 2, 3). It is also known that endovascular myocardial reperfusion gives the most optimal results in this patient population compared with alternative treatment options for blood flow restoration in the infarct-related artery. However, in some cases there is a mismatch between angiographic results of endovascular interventions (adequate elimination of obstacle for the blood flow in the IRA, lack of the residual stenosis, signs of serious intimal dissection, opacification of the whole vessel) and clinical and laboratory parameters of the disease (continuing pain or its recurrence, insignificant *ST*-segment resolution on the electrocardiogram, infarction area expansion by EchoCG). Therefore, complicated clinical course of the disease is observed in the immediate post-operative period accompanied with both worsening in functional status and functional capacity of the left ventricle (4). The reasons for this mismatch between EVI results and clinical data, in the majority of authors' opinion, are to be searched for myocardial perfusion disturbances at the microcirculatory level which are difficult to verify using selective coronarography. (Fig. 1).

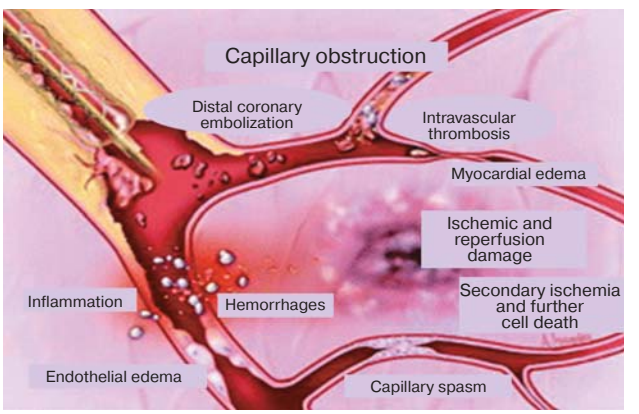

Figure 1. Vascular microembolization and its potential consequences caused by EVIs in AMI patients (adapted from J. Ronen et al. Circulation. 2008; 117: 3152–3156).

These myocardial perfusion disturbances may be related to possible distal embolization of the coronary vessels with fragments of thrombus occluded the IRA. It may be a clinical reason for the variety of cardiovascular complications, including mortality, in these patients (4, 5).

Unfortunately, the clinicians have no possibility to assess correctly myocardial perfusion and microcirculation in urgent conditions, as all myocardial reperfusion interventions in AMI patients are performed urgently. Therefore, indirect methods and criteria for assessment of myocardial perfusion of the left ventricle of the heart are used commonly. They include: TIMI blood flow assessment; myocardial perfusion by MBG; *ST*-segment resolution evaluation.

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Article received on December 20, 2013.
Accepted for publication on January 14, 2013.

Table 1. TIMI blood flow

TIMI 0 (no perfusion)	No antegrade contrast medium beyond an occlusion.
TIMI 1 (minimal perfusion)	A small portion of antegrade contrast medium passes beyond the occlusion, with incomplete filling of the distal IRA segment.
TIMI 2 (partial blood flow restoration)	Contrast medium passes an occlusion and fills the distal IRA segment, but its filling and emptying is delayed compared with the proximal segment of the IRA.
TIMI 3 (complete blood flow restoration)	Normal antegrade blood flow beyond an occlusion

Table 2. Blood flow by MBG scale

MBG 0	No myocardial perfusion.
MBG 1	Perfusion is registered during the contrast medium administration and disappears just after contrast medium flushing from the main coronary artery.
MBG 2	Perfusion is registered during the contrast medium administration and within <3 cardiac contractions after contrast medium is flushed from the main coronary artery.
MBG 3	Perfusion is registered during the contrast medium administration and within >3 cardiac contractions after the contrast medium is flushed from the main coronary artery, and it disappears prior to the next administration of the contrast medium.
MBG 4	Perfusion is registered during quite a long period, and it does not disappear completely prior to the next administration of the contrast medium.

Blood flow in coronary vessels by TIMI scale:

It is the most common method to assess the blood flow in the large epicardial coronary arteries (6-7). Initially, this classification included angiographic assessment of blood flow restoration in the IRA in AMI patients after thrombolytic therapy had been used. However, it has further become widely used to assess the efficacy of endovascular interventions in relation to the introduction of EVIs in the clinical practice (Table 1).

Therefore, this classification includes assessment of blood flow in the large epicardial arteries, without regard to microcirculatory vessels; however, the distal embolization of the large branches (so-called macroembolization) may be assessed using this sclae (8).

Moreover, based on this scale it is possible to determine a so-called no-reflow phenomenon, when the contrast medium floats without washing out in the IRA bed. It should be noted, that the EVI site looks typical in this situation, but the main problem is the difficulty of adequate blood/contrast medium drainage at the level of microcirculation. The reason for this phenomena is not clear enough, although most authors lean toward the idea concerning the massive distal embolization (Fig. 2) and/or considerable arteriole spasm.

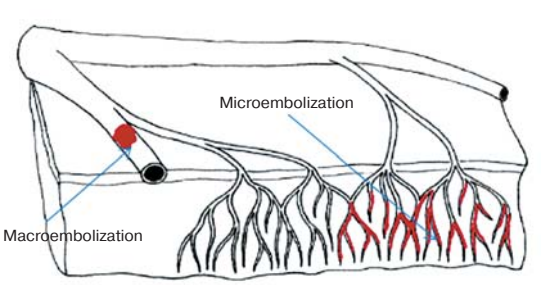

Figure 2. Micro- and macroembolization (adapted from EPCR 2009, G. Olivecrona).

Myocardial perfusion assessment using MBG:

In the course of time, particularly when a special attention was paid to the no-reflow phenomenon and distal microembolization, it became obvious that TIMI scale does not meet all requirements for EVI efficacy, and especially does not allow for assessing myocardial reperfusion at the microcirculatory level. Meanwhile, researchers paid their attention to the fact that pattern of intensive myocardial opacification followed by cardiac veins opacification within 4–8 cardiac cycles was observed during coronary angiography with prolonged exposure in AMI patients with good results of endovascular interventions and with no signs of distal coronary bed embolization. On the other hand, AMI patients with suspicion for distal embolization after EVI had no pattern of contrast penetration into the myocardium or it completed significantly faster; this suggested the blood bypassing the capillaries. Several classifications for angiographic assessment of myocardial perfusion in the IRA area were suggested based on this phenomenon (9). Myocardial Blush Grade is the most common (Table 2).

Table 3. Classification of *ST*-segment resolution

No resolution	Reduction of *ST*-segment in the infarct-related leads <30%.
Partial resolution	Reduction of *ST*-segment in the infarct-related leads varies from 30% to 70%.
Complete resolution	Reduction of *ST*-segment in the infarct-related leads >70%.

Table 4. Thrombosis classification in AMI patients (From J Invasive Cardiol. 2010)

Grade 0	No thrombus.
Grade 1	Possible parietal thrombus.
Grade 2	Small thrombus <0.5 IRA diameter.
Grade 3	Intermediate thrombus of approximately from 0.5 up to 2 IRA diameters.
Grade 4	Large thrombus >2 IRA diameters.
Grade 5	It is impossible to assess thrombosis severity due to recent and complete IRA thrombotic occlusion.

This method requires careful assessment of the final angiogram, at least in two views. The proper conduct of this exam allows for identification of distal microembolization, which, in turn, may be a prognostic test repeatedly proven in the large randomized trials (Fig. 3).

Assessment of ST-segment resolution

The next method of myocardial perfusion assessment is an electrocardiographic one based on ST deviation before and after EVI in the ECG leads corresponding to myocardial infarction (10). Although this criterion is not based on angiographic data, it demonstrates changes (reduction or persistence) of myocardial ischemia in the infarct-related area with a high level of significance and may likely suggest the presence or absence of distal embolization. Conventionally, the magnitude of ST depression after EVI is classified into three grades (Table 3).

The time period for which ECG should be evaluated, is not determined clearly, but in the majority of cases this period is reported to be from 60 to 180 min after EVI. This parameter with a high level of significance correlates with immediate and long-term prognosis (Fig. 4).

Angiographic assessment of thrombosis in the IRA bed:

AMI is known to be associated with rupture of the unstable atherosclerotic plaque and thrombosis of the IRA lumen in 98% of cases (11). Detailed histological examination of this process has proved a heterogeneity of each specific clinical case. Thus, a considerable stenosis of the IRA and relatively small thrombotic masses were noted in some cases; in other cases, on the contrary, atherosclerotic plaque of small volume and a massive thrombus were observed. In the context of EVI, the last option is less favourable, because a large thrombus in the site of intended stenting is likely to cause distal micro- and macroembolization. Therefore, the following Thrombus burden score (TBS) classification, which was developed in 2010, is based on angiographic assessment of thrombosis in the IRA lumen (Table 4).

If Grade 5 thrombosis is revealed during the angiography, the authors recommend a predilation using a balloon 1.50 mm or less in diameter for assessing thrombosis severity. In accordance with authors' conclusions, Grade 4 thrombosis is an independent marker for

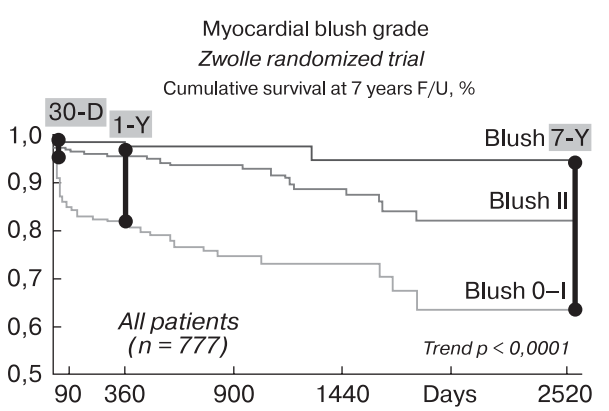

Figure 3. Long-term survival of AMI patients after urgent EVIs depending on myocardial blush grade (MBG) (adapted from Van't Hof et al. Circulation 1997).

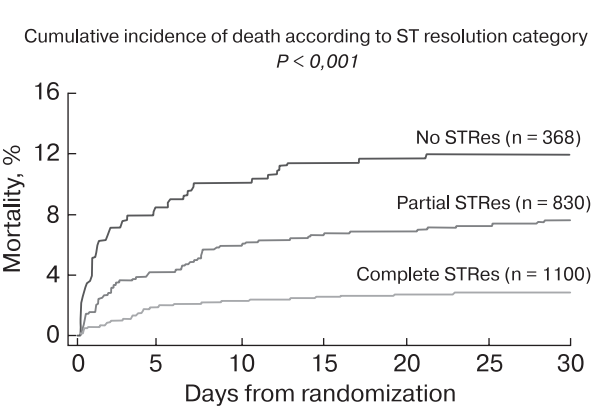

Figure 4. Mortality in AMI patients depending on *ST*-segment resolution (180 min after EVI) (adapted from Scirica B.M. et al. Eur. Heart. J., 2007).

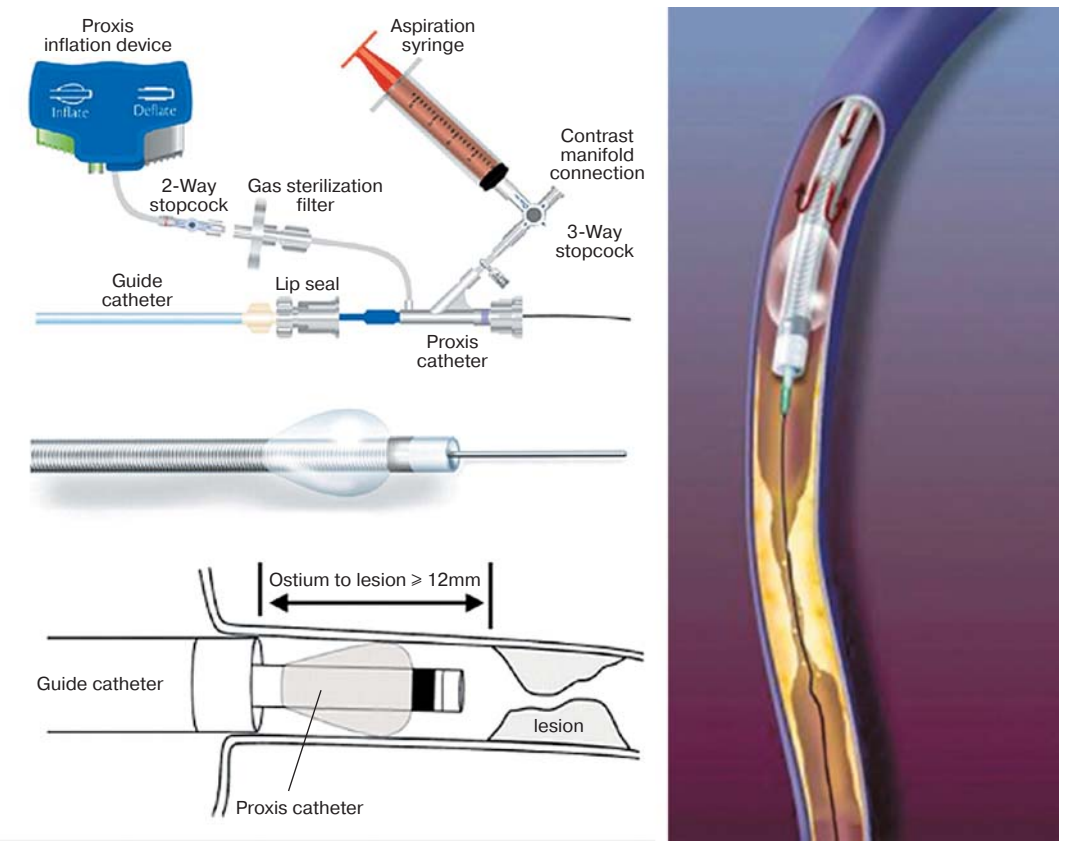

Figure 5. Basic design of the PROXIS catheter (adapted from Cardiovascular Interventions 2011, 4, 8).

unfavourable prognosis in the long-term period in AMI patients who underwent urgent EVIs.

Thus, distal micro- and macroembolization is a serious adverse process complicating the course of acute myocardial infarction and unfavourably affecting its prognosis. Therefore, clinicians have focused their efforts on searching for effective preventive methods against multi-level coronary embolization with fragments of thrombus during endovascular procedure. Various pharmacological and mechanical methods for distal protection were tested over the last decade (12–17). The whole variety of existing mechanical (drug-free) devices, preventing from distal embolization, may be divided, in our opinion, as follows:

– Proximal protection of the IRA bed;
– Distal protection of the IRA bed;
– Manual thromboaspiration;
– Mechanical (automatic) thrombus extraction.

More detailed description of these methods and thier application results in patients with acute myocardial infarction are provided below.

Proximal protection of the IRA bed

The proximal protection of the IRA is based on the balloon dilatation proximal to the target lesion; at that time, the antegrade blood flow is blocked, and stenting is performed through its internal lumen (6 Fr). The Proxis balloon catheter may be used for this purpose. After that, a certain amount of blood and existing emboli are aspirated from the IRA. Then the balloon is deflated and the Proxis catheter is removed (Fig. 5).

The advantages of this system are as follows: I) protection of the distal bed before the wire penetration through the target lesion; II) protection of the side branches and collaterals from potential embolization; III) possibility to replace the coronary wires not removing the device. After balloon inflation, the device has a supporting function and facilitates endovascular intervention.

The disadvantages of this method are: I) impossibility to use it for ostial lesions and proximal lesions of the coronary arteries; II) antegrade blood flow is stopped in the IRA during an intervention; III) unwieldiness of this system.

Currently, there are few trials designed to investigate the efficacy of this system in AMI patients. The largest of them is PREPARE (12), in which no obvious benefits from this device were demonstrated compared with control arm in AMI patients who underwent urgent EVIs

Figure 6. Basic design of FilterWire distal protection system (adapted from Cardiovascular Interventions 2011, 4, 8).

Figure 7. Basic design of PercuSurge system (adapted from Cardiovascular Interventions 2011, 4, 8).

Figure 8. Basic design of ELIMINATE catheter for manual vacuum thrombus aspiration (adapted from www.terumo-europe.com).

without proximal protection of the IRA. Moreover, no significant effect on mortality and 30-day recurrent AMI rate were reported. However, *ST*-segment resolution was more complete in the study group compared with the control one; it may indirectly predict the better restoration of the microcirculation in AMI patients when the PROXIS system is used. Therefore, the efficacy of this system remains disputable, and further investigation of this issue is required.

Distal protection of the IRA bed

Several systems have been developed for distal protection of the IRA bed. They include both placement of filters on the wire distal to the intervention site (Fig. 6), and distal inflation of soft silicone balloon in the IRA lumen (Fig. 7).

While the idea to protect the IRA from distal embolization is attractive, its practical realization did not provide the desired effect. Several trials (Dedication study 626 filter wire, Diplomat trial 52 Angioguard, Promise trial 200 filter wire, Asparagus trial 341, Emerald trial 501) designed to study these systems in the coronary arteries of AMI patients reported advantages for neither prognosis nor AMI size (3, 4, 12, 13, 21). The total number of patients exceeded 1500. Therefore, the distal protection demonstrated no considerable efficacy in AMI patients who underwent urgent EVIs.

Manual thrombus aspiration catheters

This is the most common class of devices, which are currently widely used to prevent from distal embolization in AMI patients while urgent EVIs are performed. To date, there are more than 20 types of manual thrombus aspiration catheters. The mode of it action is to create negative pressure at the distal tip of catheter at the moment of penetration through the target lesion, using a syringe at the proximal tip of the device (Fig. 8).

It should be noted that in the first trials (REMEDIA, PHIRATE, DEAR-MI) (2) concerning efficacy of the thromboaspiration procedures, no considerable advantages were revealed compared with the standard endovascular myocardial revascularization without accompanying thrombus extraction (13, 19). Worsening of blood flow in the IRA and decreased left ventricle function were even observed in some studies. In our opinion, these results might be firstly related to the imperfection of the devices (lumen of the first catheters was small and did not allow removing completely the thrombus masses from the IRA, and, on the other hand, very large external diameter of catheter might also promote the thrombus fragmentation and

Figure 9. Basic design of AngioJet catheter for mechanical thrombus aspiration (adapted from AM ? Cardiol 2002; 89).

embolization with the thrombus parts of the distal coronary vessels). At the beginning of these studies, the investigators naturally had no sufficient experience with such devices. Thereafter, as a result of significant improvement of devices for thrombus extraction and accumulation of experience, the results became better and it was confirmed in the large, multicenter, randomized study TAPAS (2008) (14, 20), where the superiority of manual vacuum thrombus aspiration over the routine IRA angioplasty was proved in the great number of AMI patients. This concerned both immediate and long-term angiographic and clinical outcomes (21, 22). Thereafter, the results of this study were confirmed by the variety of large randomized studies and, as a consequence, the new devices for vacuum thrombus aspiration became available.

The improvements of the next generation of manual thrombus aspiration catheters concerned more safe and effective manual removal of thrombi and restoration of coronary blood flow. Thus, for instance, to assess the immediate results the catheter was upgraded with a framework membrane for thrombus extraction and a convenient syringe with a fixed plunger to create permanent exhaustion at the distal tip of the catheter. Moreover, visualization of the distal tip of the catheter was also improved, along with the control over thrombus extraction process; the characteristics of catheters were upgraded: inner lumen became larger, outer diameter became smaller, the catheters became coated with hydrophilic substance to reduce friction during thrombus extraction. The development of these catheters resolved these problems, which was reflected in the recent trials (EXPIRA, VAMPIRE, TAPAS (14, 20, 21)). In all these trials, utilization of manual vacuum thrombus extraction catheters during urgent EVIs in AMI patients had a positive effect on the primary outcomes, patient prognosis and reduced myocardial infarction size in the study arm compared with the control arm. Just results of these trials allowed the American College of Cardiology (ACC/AHA) to replace recommendation class 2B with 2A.

Mechanical (automatic) thrombus extraction

The next class of devices which are especially noteworthy, is mechanical (automatic) thrombus extraction systems such as: Angioget; X-sizer; Rescue; TVAC etc. The mode of their action is based on the Bernoulli principle: vacuum is created in the area where the rate is maximal and the pressure is minimal. Saline stream creates a low-pressure area while expanding inside the special catheter with a rate of approximately 150 m/sec in the direction from the catheter tip. In-vessel thrombus passes from high-pressure area to low-pressure area through special holes and transfers to a special collecting package (Fig. 9).

Therefore, theoretic backgrounds for thrombus extraction from the IRA were considered favourable, especially as this device was upgraded some years ago and its dimensions and deliverability of the applied part of the catheter were considerably improved.

Indeed, the initially small randomized trials demonstrated positive results of these devices for rheolytic thrombectomy in AMI patients. Thus, for instance, Nakagava et al. (19) reported successful results of AngioJet used in 31 AMI patients prior to IRA stenting. In a single-center trial, Singh et al. (23) reported thrombus extraction using AngioJet in 72 patients with an apparent thrombus in the IRA. In spite of high risk of EVI, the results of these devices were impressive: the success rate of procedure was 93%, one patient died at in-hospital stage, and 1-year mortality was 10% (10). Taghizadeh et al. (23) also reported the efficacy of AngioJet system and stenting in AMI patients with cardiogenic shock. The success rate of procedure was 95%, and final TIMI 3 blood flow was achieved in 89% of cases.

However, optimism was replaced with vigilance in relation to this device when the results from the large multicenter randomized prospective study (AiMI) (24) were published. In this study, the device for rheolytic thrombus extraction did not reduce infarct size, but even increased cardiovascular complication rate within 30 days after myocardial infarction (Figs. 10, 11).

The further detailed analysis of reasons for such deplorable results led to the following conclusion: the mechanical thrombus extraction in AiMI trial was performed routinely not

based on the TBS parameters, whereas in the previous studies AngioJet was used only if TBS was ⩾ 3 (in AiMI trial, less than 20% of patients had TBS > 3).

The advantage of AngioJet used in patients with AMI and high grade of TBS was confirmed in the recently reported large randomized trial JETSTENT (25), in which 501 AMI patients were included. The cardiovascular complication rates in 1 month after myocardial infarction were 3.1% in the main group versus 6.9% in the control group (p = 0.05), in 6 months – 11.2% versus 19.4%, p = 0.011, in 1 year – 14.9% versus 22.7%, p = 0.036.

Therefore, based on the literature data, it may be concluded that rheolytic thrombus extraction is more preferable in AMI patients with high TBS grade than routine intervention, and gives more favourable clinical and angiographic results both in immediate and long-term period. Additionally, some authors (26), based on their experience and meta-analysis results, propose their own algorithm for interventional procedures in AMI patients.

The above algorithm for EVIs in ACS patients, in our opinion, is fairly rational; at least, its application assumes a certain standardized approach to devices for aspirating thrombi from the sign-related artery; however, additional randomized trials are required for its final approval and efficacy assessment.

In summary, it should be noted that main types of systems for myocardial protection from distal embolization used during urgent endovascular intervention in ACS patients have led to heterogeneous outcomes. Thus, the proximal balloon protection demonstrated unfavourable results compared with IRA angioplasty (stenting) alone. The results of entrainment filters placed distal to the angioplasty area, as well as distal balloon were similar to the efficacy of urgent endovascular interventions without these devices. Such mechanical devices for thrombus removal from the infarct-related artery, as Angiojet etc. are less available compared with the preceding ones, because they require special equipment; the results of their application are controversial and require further investigation. To date, in our opinion, the most preferable in terms of availability and efficacy are devices for manual vacuum thrombus extraction (such as Eliminate, Diver, Export), which, in the vast majority of cases, help to prevent from distal embolization of the IRA and, thereby, to preserve its microcirculatory bed and to provide adequate reperfusion of infarcted myocardium after endovascular interventions.

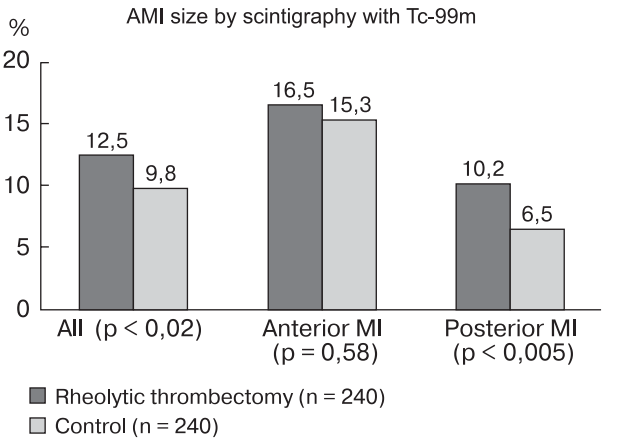

Figure 10. Assessment of AMI size by scintigraphy in AiMI trial (adapted from J. Am. Col. Cardiol. 2006, 48, 244).

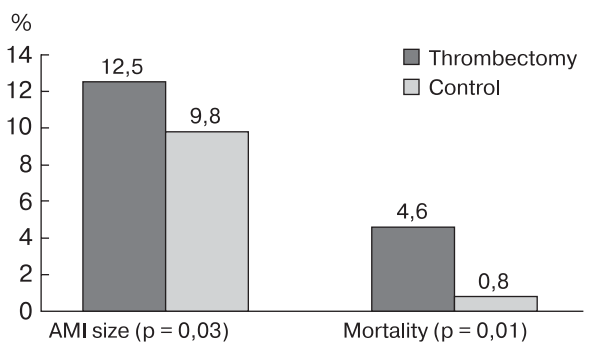

Figure 11. Mortality and MI size within the period from 14 to 28 days in AiMI trial (adapted from J. Am. Col. Cardiol. 2006, 48, 244).

Table 5. Indications for thrombectomy in AMI patients

In what kind of AMI patients EVIs should be supplemented with thrombectomy?		
0 1	No thrombosis Possible thrombosis	Direct stenting (50%)
2 3	Small thrombosis, vessel lumen diameter <0.5 Intermediate thrombosis, vessel lumen diameter from 0.5 up to 2	Manual thrombectomy (25%) + stenting
4 5	Large thrombosis, vessel lumen diameter >2 Acute thrombosis (fresh thrombosis)	Thrombectomy using AngioJet (25%) + + stenting +Abciximab
6	Chronic total occlusion	

Finally, it should be recognized that any of above mentioned devices is highly effective when an intervention for stunned myocardium is complex (pharmacological and invasive coronary procedure), because it prevents from reperfusion myocardial damage and apoptosis.

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Summary of the Conference "MODERN TRENDS IN THE TREATMENT OF STEMI" (Moscow, November 8–9, 2012)

15th anniversary of Moscow City Center of Interventional Cardioangiology and 90th anniversary of the world-renowned scientist, one of the founders of Soviet-Russian school of cardiac surgery Vladimir Bourakovsky... By cold Moscow November and in a warm friendly atmosphere these two dates, so different and so far apart in the layman's terms, have brought together the colleagues, the friends and the "comrades in arms" from various regions of our country, the USA, Italy, Latvia, Spain and Germany – the leading specialists in the field of the treatment of acute coronary disorders.

The organizer and the initiator of this event was Moscow City Center of Interventional Cardioangiology, the institution conceived by Professor Vladimir Bourakovsky and created by his pupil Professor David Iosseliani 15 years ago, with the support and the assistance of top managers of Moscow and the federal-level politicians – Yuri Luzhkov and Evgueny Primakov. Fifteen years of intense and self-dedicated work, thousands of saved lives, dozens of formed specialists who became heads and workers in many departments of endovascular surgery in Moscow hospitals – such is the brief summary of the activities of this unique institution, whose structure and trends have anticipated current program of modernization of Russian medicine. The team-oriented professional staff of the Center under the guidance of David Iosseliani, being the acknowledged leader in the treatment of patients with acute myocardial infarction, continues to scale new heights in the search and inculcation into the clinical practice of the newest and the most effective techniques of management of cardiologic patients.

The Conference opened to the strains of a violin ensemble. During the opening ceremony the representatives of the city government and of the management of city healthcare greeted the participants of the forum. The opening plenary session, as well as the final session were dedicated to the memory of Vladimir Bourakovsky. The audience warmly greeted the members of Bourakovsky's family, his friends and colleagues. The lectures of Professors D. Iosseliani, V. Chekanov, Yu. Volynsky with the recollections about the great physician, researcher and friend aroused a vivid interest of the audience.

The scientific program of the Conference was focused, on the one hand, on the lectures of world-renowned leaders of cardiology concerning the key problems of organization and conduction of therapeutic interventions in patients with acute myocardial infarction, and, on the other hand – on live case demonstration from the cathlab of Moscow City Center of Interventional Cardioangiology. The speeches have been interrupted by live stand-ups, and the audience as well as the participants of Round-table discussions could follow in online mode the course of urgent endovascular procedures performed in patients with AMI who had been brought to the center by emergency teams. The unique opportunity to participate in primary procedures of endovascular reperfusion and to discuss their technical details and pharmacological support in online regimen was a clear proof of high level of training of invasive cardioangiologists and specialists in cardiac intensive care. The article of Anthony N. DeMaria, the Editor-in Chief of the Journal of American College of Cardiology (1), written without delay, is the most emotional and lively reaction on the event. The author describes his satisfaction with high professionalism of Russian cardiologists who use in their everyday practice the whole spectrum of modern technologies.

The experience with primary PCI, the results and the perspectives of the development of interventional cardiology in various regions and countries were presented by Russian cardiologists David Iosseliani (Moscow) and Boris Shakhov (Nijny Novgorod), Eulogio Garcia (Spain), Cindy Grines (USA), Andrejs Erglis (Latvia), Werner Haberbosch (Germany).

Among the most thrilling problems discussed by the participants and the experts one

can mention the problems of the choice of the most optimal stent for the treatment of AMI, of the evaluation of the results and the horizons of transcatheter aortic and mitral valve replacement – lectures of Antonio Colombo (Italy), of the determination of stem cell role in the management of AMI – lecture of A.DeMaria (USA).

Two dates falling far apart and however so close, the colleagues from different – so far off and so close countries – who have joined their efforts in the formation of common approach to the fight against one of the most serious disease threatening today's mankind – against acute myocardial infarction…

On behalf of the organizers of the Conference we want to express our gratitude to all the participants: the speakers and the audience, the management and the staff of Moscow First-Aid Station named after Puchkov, the cardiologists and the interventionists of Moscow City Center of Interventional Ccardioangiology who have performed successful interventions in online regimen. We are deeply thankful to the management of Moscow Department of Healthcare and personally to Professor Georgy Golukhov for their support and assistance in the organization of the Conference. Special thanks to the companies manufacturing medical equipment and medications for their sponsorship: to our General Sponsors "Cardiomedics", "Medtronic", "Abbott Vascular", our Main Sponsors – "Biotronic", "Invamed", "Johnson & Johnson", "Raut Business", "Terumo", our Sponsors – "Astra Zeneca", "Bayer AG", "Boehringer Ingelheim", "B.Braun Medical", "Biosensors", "Briz Medical", "EgaMed", "Implanta", "Cardex", "Cardioline", "Xanta Medica", "GE Nycomed", "Paritet", "Pfizer", "Raymed", "Raypharm", "Siemens". Thanks to our welcoming hosts from Moscow World Trade Center, whose assistance made it possible to conduct our forum at the highest organizational and technical level.

We are sure that in the new year 2013, we shall meet again, in order to share the accounts of our new achievements, and we are looking forward to cooperate with all the colleagues working in the field of complex pharmaco-endovascular approach to the treatment of AMI. At present our Organizing Committee initiates the organization of the first Moscow registry on Acute Myocardial Infarction. Besides, we are looking forward to receiving your suggestions and ideas for the conduction of the First Annual International Course "Modern Trends in the Treatment of STEMI – from Guidelines to Everyday Practice" (with continuous live-case demonstration of endovascular management of AMI), to be held in Moscow on September 26–27, 2013.

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Vladimir Bourakovsky: prominent cardiac surgeon and organizer of medical science and practice. His role in creation of Scientific and Practical Centre of Interventional Cardioangiology

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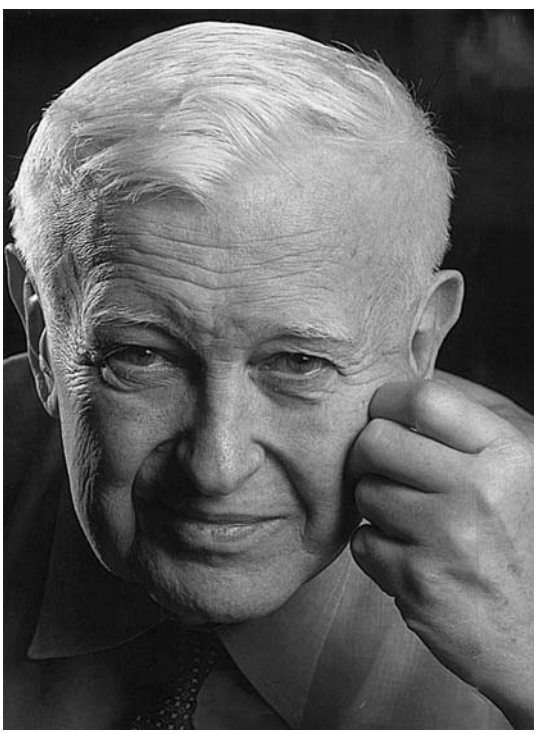
Looking back at the life journey, you certainly remember people whom you have met, communicated, worked and been friends with. It is clear that the most brilliant and interesting people, who somehow have left a deep indelible imprint on your life, remain memorable. Professor Vladimir Bourakovsky is at the top of the list of such people. It can be declared with full responsibility that he was an outstanding person and a prominent leader.

It is very interesting to spend time with such people as he was; they are the engines of progress, although, sometimes it can be very hard as they are extremely demanding and, respectively, exhausting and tiring; you often want to tell them to get lost, but it is very sad without them, you feel dreadful boredom, emptiness. Unfortunately, when they are gone, you begin to understand how much has been lost and to realize how much they have done. And the farther they get, the better it is noticeable.

And this is how the great Bourakovsky has arisen: On a usual scorching August day of 1922 in one of the numerous, but unique in its originality and beauty, small side streets of old Tiflis, a son of Russian intellectuals, the boy, who was destined to become an eminent scientist, surgeon and citizen in the future, Vladimir Bourakovsky, was born. But all of this would happen later, and meanwhile Vova (this was his nickname) was growing in the same way as thousands of Tbilisi boys who were receiving "primary education" in picturesque yards and



Professor Vladimir Bourakovsky (1922–1994)

streets of the southern city. Here he felt the bitterness of early loss of his father, but here as well he experienced a remarkable spirit of neighbourliness and friendliness, purely Tbilisi spirit, which helped Vova and his mother Mariya, with whom I was well acquainted, to overcome difficulties during their life journey. Later, Bourakovsky in a circle of his loved ones would repeatedly recall episodes from his life in Tbilisi which played a considerable part in his evolvement as a person and individual. Here as well, in Tbilisi, he graduated from Tbilisi State Medical University and took his first shy steps in the clinic, headed by D.G. Iosseliani, Senior. Communication between the teacher and the student further resulted in a great and moving friendship. Vladimir Bourakovsky always especially noted that he was lucky in everything

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Manuscript received on November 12, 2012
Accepted for publication on December 5, 2012

Hanting and Fishing –
two beloved hobbies of V. Bourakovsky.

regarding teachers. The same happened in Leningrad, where he mastered his skills in the clinic headed by the prominent Soviet surgeon Petr Kupriyanov; he was also lucky in Moscow where during the different time periods he worked under the guidance of eminent Soviet surgeons Alexander Vishnevsky and Alexander Bakoulev. However the teachers, who saw a man of outstanding abilities in front of them, a wonderful scientist, surgeon and a loyal successor to traditions of Russian and Soviet surgery, were lucky as well. Already in 1953, when V. Bourakovsky was a little older than thirty, academician P. Kupriyanov on a day of 155th anniversary of the Military Medical Academy was talking in his report about Bourakovsky's substantial contribution to the development of thoracic surgery. And, of course, the star of Bourakovsky most brightly shined when he joined the Institute of Cardiovascular Surgery, which he headed till the end of his life. Starting from that period, a qualitatively new stage in the development of cardiac surgery has begun in our country, which led the Russian cardiac surgery school to a worthy place among other international schools. Of course, when revoking the memory of Vladimir Bourakovsky, first of all, he should be remembered as a prominent cardiac surgeon and cardiologist, a scientist; but I would like to note that those who have not seen Bourakovsky among friends, at the festive table, in the hunting field, at the book shop or reciting favorite poets, cooking in the kitchen, helping the loved ones in trouble, courting the ladies – believe me, those people cannot say that they knew Vladimir Bourakovsky well.

He had an incredible charisma. His slightly narrowed cornflower-blue eyes had magic effect on the conversation partner, and in combination with soft, cushioned, singsong, and unexpectedly high-pitched voice, making compliments, they were completely charming the person he was talking to. I often witnessed how he convinced different high-rankers that it was important and necessary to buy an expensive medical equipment, to build a new building, or, after all, to send the staff members on a business trip somewhere abroad. He was doing this in such a way that he would always win. When he was passionately telling about some new or complicated surgery, he always had a pencil and paper at his fingertips, and he traced some kind of scribbles, understood by him only, trying to show the course and the results of the surgery. All of this was outside the box, unusual and maybe even incomprehensible for some people. There was no brass plate on his office door saying: "Visiting hours: from __ to __". His doors were always open for everyone equally. There were always a lot of people in his reception office, he always had kind words for them and he was always able to provide care.

It was typical for Bourakovsky's decisions and innovations to be ahead of time. Things that the majority of people surrounding him considered unreal and somehow illogical, were evident and absolutely logical for him. Looking back at our recent past, one can remember a lot of innovations implemented by Professor Bourakovsky despite resistance, unwillingness or indifference of many of us, which nowadays appear to be an everyday reality. Think, for instance, of mathematical modeling in cardiovascular surgery. How much effort it took him to implement all of this into clinical practice and to overcome the resistance, coming from a certain part of medical personnel. After all, in fact, I am talking about so needed automated case history suitable for complex mathematical analysis of complex quantitative parameters; it is unlikely that nowadays any one can get along without it.

Probably, something similar happened with his idea of creating a service on the basis of

multi-field city hospital, providing specialized high-tech medical care to the patients with various forms of coronary artery disease, particularly focusing on the patients with acute forms of the disease. We were all wondering why the service should be set up specifically on the basis of the city hospital, and not at the Bakoulev Institute. There was even a thought, and some resentment as well, that, in a manner of speaking, he wanted to deport us far away out of the sight. Especially since the first steps of the coronary surgery in the seventies were not quite confident, there were failures, deaths, and not everything was going the way we wanted. These were the reasons for doubt. But in fact it turned out that exile had nothing to do with it. Vladimir Bourakovsky had his own reasons which, as the future showed, were absolutely right.

The first and the most important argument in favor of creating a service outside the Institute was as follows: a lot of scientific investigations and know-hows of scientific research institutes did not get to the practical healthcare in those days. It was no secret for any of those who worked during that time in the medical field, that according to tradition in our country established since the Soviet era, research studies, as well as development of new treatment methods were concentrated at the scientific research institutes under the federal control, i.e. under the auspices of the Ministry of Health Care or the Academy of Medical Sciences. In this article I will not dwell on how effectively and cost-efficiently such system operated, overall, and separate Scientific Research Institutes, in particular; however, the one thing was clear even then – namely, that the latest innovations of medical science, as well as developments in high-tech medical technologies were implemented into practical health care belatedly and extremely slowly. Often, this did not happen at all. To a large extent, the reason for this was disunity that existed between Scientific Research Institutes, which were subject to federal control, and practical medical institutions which were and are subordinated to municipal boards. Meanwhile, a close relationship between Scientific Research Institutes and hospitals was a vital necessity. Both specialists and health professionals understood this (although the latter understood this to a much lesser extent, or pretended that they did not understand, due to many reasons, mainly due to their passivity and partially due to incompetence regarding everything new happening in the medicine field). Significant underfunding of the health care, unfortunately, typical for our state, was heavily interfering too. Nevertheless, even back then there were enthusiasts who, despite all obstacles, were trying to make the relationship between science and practice more effective and productive. First of all, of course, such leaders of national health care as Vladimir Bourakovsky, who in the late seventies of the last century already understood the urgent need for the close relationship between Scientific Research Institutes and city hospitals, were among them.

This served as one of the most important arguments when Bourakovsky made a decision to establish the coronary service outside the Institute, which at that time had only 140 beds for the newborns, infants and elder children; for acquired valvular heart diseases and vascular pathology; for pacemakers and other rhythm disturbances, and finally, for the coronary patients. Obviously, these beds were not able to fit a quite large flow of patients with acute coronary pathology. Bourakovsky realized that either this service had to be open for the acute patients 24 hours all seven days a week, or this service would never amount to anything. Fully functional 24-hour cardiac intensive care unit and coronary angiography service were important in order to succeed.

Another important argument in favor of multi-profile hospital was, in particular, its versatility. After all, we all are well aware that the patients with acute coronary artery disease often suffer from a variety of other associated diseases which may worsen at any time, and that they may require, at least, the consults of different specialists, not to mention transfer to other units.

It should be noted that Bourakovsky's decision to establish a service on the basis of a city hospital did not necessarily mean that everything would be exactly this way. Consent from Moscow authorities and municipal health care authorities was required. Believe me, it was not an easy task. Only persistence and the influence of Professor Bourakovsky allowed us to solve this problem. I witnessed how many difficulties and bureaucratic obstacles he had to overcome on his way to create this service. I remember meetings of Bourakovsky with the head of Municipal Health Care Administration of that time, Mr. Vorokhobov, who was a clever and experienced health official, and a friendly person as well; however, it was so difficult to prove him the importance and significance of

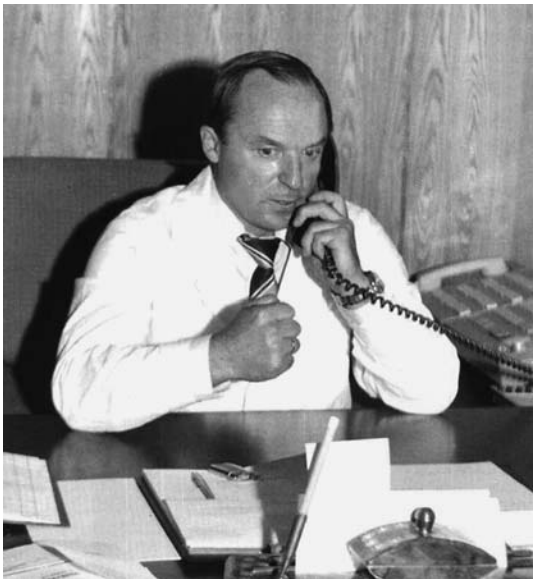
L.A. Vorokhobov

Professor Vladimir Rabotnikov (on the right)

creating such symbiosis on the basis of a city hospital. But, in spite of everything, this service has been established, and for many years of its existence it has proven its usefulness and effectiveness in the treatment of patients with cardiovascular diseases. In the end, after many mutual approvals we were referred to the City Clinical Hospital No.53 in order to create such service. A lot of people do not know or have already forgotten long ago that this whole saga with a coronary service has begun not at the City Clinical Hospital No.15, but at the City Clinical Hospital No.53. I would not dwell for very long on our stay in that hospital, because, regardless of a rather hearty welcome, provided to us by the hospital staff and administration, we quickly realized that this was not a hospital, required for creating a modern service providing high-tech medical care to the coronary patients. The hospital was already old, and kind of densely populated, without corresponding cardiologic and cardiosurgical medical equipment, and obviously without cardiac catheterization laboratory and cardiosurgical operating rooms. Unfortunately, I have not kept the photos of those premises in which we were accommodated, but believe me, you would not admire them. After all, we were planning to create the first service in the country, where, according to the figural expression of Professor Bourakovsky , cardiac intensive care unit for the patients with acute myocardial infarction, cardiac department, cardiac catheterization department, cardiac surgery department and cardiac rehabilitation department should be united in “one cluster”. Professor Vladimir Rabotnikov was appointed as the head of that whole service, and I, as his deputy, had to run the cardiologic service. These were the plans of our administration, and these were the plans of Bourakovsky, but in fact we received one department with 60 beds, which was called the Department of Cardiovascular Surgery; however if therapeutic cardiac patients who were treated there, had indications for coronary angiography, were transported to the Bakoulev Institute and brought back to the hospital after the investigation. Those who required an operation once again were transferred to the Bakoulev Institute, where all the surgeries were performed. Back then we did not conduct angioplasty of the coronary arteries. Our stay in that hospital lasted approximately for one year, and it could last for a long time, if not for an accident.

By that time, building of a very modern, according to the standards of that time, multiprofile hospital, established with the assistance of the First Secretary of Moscow City Committee of the Communist Party of the Soviet Union Victor Grishin, in a new rather green Moscow district had been completed. It was his gift to the voters, as he was elected to the Supreme Soviet of our country right from that district. However, the most important was not this, but the fact that the former (by that moment) head physician of our hospital No.53 was appointed as the head physician of the City Clinical Hospital No.15 (this number was assigned to the new hospital). And so the new head physician whose name I revoke with a great respect and words of gratitude, Vladimir Mudrak, offered us to move with him to a new hospital. Professor Bourakovsky, just as we all,

gladly accepted this offer, because it was a completely different level and, most importantly, the hospital was new, and we could equip the department based on our own preferences and taking into consideration modern requirements. We received 130 (65 cardiac and 65 cardiosurgical) beds and also separate cardiac intensive care units for acute coronary patients (6 beds) and for cardiosurgical patients (also 6 beds). In order not to repeat the structure of this service again, I would just say that Rehabilitation Department (60 beds) was later added; X-ray surgical department appeared very soon, as well as, a little bit later, Department of Vascular Surgery (60 beds) headed by Doctor Yuri Grozovsky. One can say that by 1982–1983 the service began working the way it was designed to work by Vladimir Bourakovsky. It should be noted that during this period the emphasis was laid on surgical myocardial revascularization, while balloon angioplasty was still in its embryo state, and there was no stenting at all. However, that period did not last long, because we experienced big problems with intra- and postoperative complications in patients with acute myocardial infarction (in particular, hemodynamic complications). However, the main problem was that the operations were performed significantly later than the term during which the patients with acute myocardial infarction could benefit from reperfusion – namely, in the first 6–8 hours after the disease onset. We realized that after expiration of this time limit all hybernating myocardium might be irreversibly dead. And we could not practically manage to perform surgeries earlier. Thus, we rather quickly abandoned the idea of a wide use of surgical myocardial revascularization in patients with acute myocardial infarction and limited these surgeries only to patients with early post-infarction angina or post-infarction heart defects. At first we started using intracoronary thrombolysis as an alternative to surgery, and since the beginning of 1988 – balloon angioplasty of the infarct-related artery. Unfortunately, it should be noted that we were facing a lot of organizational and tactical problems at the beginning. There were no guiding authorization documents permitting the use of balloon angioplasty for acute myocardial infarction, there were no standardized indications and contraindications for endovascular reperfusion, and there were huge problems with consumables. The first balloon catheters that we used were far from the optimal ones. The absence of coronary angiography teams



V.N. Mudrak

on round-the-clock duty interfered with the regular work. I confess that there even was a lack of staff for twenty-four hour shifts. I have a vivid recollection that when we started the urgent endovascular procedures in patients with acute myocardial infarction, only two people were trained to use this method – Dr. Alexey Filatov and me. Obviously, we could not provide round-the-clock daily shift at the hospital, so we were on call at home. It was an unforgettable, extremely complicated, completely exhausting, but very romantic period. Now I cannot even imagine this, but back then, upon the first phone call notifying that a “suitable” patient has been admitted with an acute myocardial infarction (the term “suitable” meant that based on his main medical characteristics he had indications for endovascular myocardial reperfusion) we jumped out of our warm beds and raced through the whole city (and back then I lived at the opposite from the City Clinical Hospital No.15 end of Moscow), and performed the necessary endovascular procedures. It was especially hard to do it in winter. And, of course, on this occasion, I would like to bow thanks to all staff members taking part in those reckless adventures. Indeed, they were the nurses and often the doctors of related specialties (for example, ultrasound experts). It is fair to say that our agony lasted not very long; the hospital administration, including the Head Physician Oleg Filatov, have done everything possible to create round-the-clock crews providing both urgent endovascular and cardiosurgical care to the patients with acute coronary blood flow impairments. They

O.M. Filatov

even had to go for certain violations, because at that time there were no regulatory documents defining the staff schedule of these services. Besides, to date there are still no such documents in a proper form. Creation of fully functional round-the-clock services was facilitated by the fact that by that time the young doctors (endovascular surgeons) had been hired, and we were able to provide round-the-clock seven days a week emergency care to the patients with acute myocardial infarction. As I have said before, at first it was intracoronary thrombolysis, then balloon angioplasty and in 1991 we performed the country's first stenting in a patient with acute myocardial infarction (1); and it may be said that around this the time we started to regularly perform endovascular myocardial reperfusion using all available at that time resources.

Back then there were not so many patients with absolute indications for endovascular reperfusion. And we did not have the right to extend indications or take any kind of risk in order not to discredit the technique. Attitude of the colleagues and health officials towards this problem for a long time was ambivalent in our country and sometimes even distinctly negative. Therefore we had no right for a mistake. Each failure would have been maximally used by our opponents. By now, most of the cardiologists, but, unfortunately, not all of them, have understood all significance and usefulness of early endovascular myocardial reperfusion, and back then the situation was different. The negative attitude of many cardiologists and health officials towards this problem was also reflected in the number of patients who were delivered to us. Ambulance units preferred taking patients to another in-patient departments, away from the "headache", or admitted patients with a late phase of myocardial infarction. We realized that something had to be done in order to drastically change the situation. It was necessary to intensify the flow of patients with acute myocardial infarction to our clinic. And here again I want to point out the perspicacity and wisdom of Professor Bourakovsky , who was able to make an agreement with the administration of "Ambulance" in order to provide our service with one cardio-resuscitation mobile team, stationed at our hospital and, in a manner of speaking, working for us. It used to receive calls from the districts nearby the City Clinical Hospital No 15 and if indicated, transported the patients with acute myocardial infarction to us, notifying us beforehand. This significantly shortened so-called "door-to-balloon" time, i.e. the time needed to prepare the patient and to deliver him/her to the operating room. Right now it all has been perfectly worked out, and back then we had to overcome difficult hardships, obstacles and opposition. Nevertheless, we still managed to beat inertness, conservatism and rigidity of thinking both of the majority of cardiologists and health officials. Of course, first of all, the credit goes to Vladimir Bourakovsky, but we also must give credit to our back then existing united team of young enthusiasts who spent days and nights at the hospital and sacrificed a lot for one purpose — to implement a fundamentally new direction in cardiology into the clinical practice of Moscow. It should be noted that during this same period we started using drip infusion of nitroglycerin for the first time in the country, although at that time the use of nitroglycerin was contraindicated in patients with acute myocardial infarction. At our own risk we purchased alcohol solution of nitroglycerin at pharmacies and administered it in infusions to the patients with acute myocardial infarction (2). This significantly decreased the incidence of severe complications and mortality in patients with this diagnosis.

Nowadays hardly anybody remembers, and I want to restore in the memory of my many colleagues that there was another emergency cardiology service (affiliated with the 2nd Medical Institute) along with us at the hospital. And so we kind of competed. In their treatment regimens they mostly used classical, conservative methods of myocardial infarction treatment, and we used endovascular and surgical methods, including the intra-aortic counterpulsation in severe patients, which was completely new for the majority of national hospitals. By the way, it should be noted that we were the first in

the country to use puncture intra-aortic counterpulsation in general, and in patients with acute myocardial infarction in particular (3). Thus, due to the use of more effective reperfusion methods of treatment, the difference in mortality rate of patients with an acute myocardial infarction between our departments was 5% in our favor. Although, it is fair to say that our mortality rate was also high according to international standards; it was 12–13%. But we must not forget that overall in the country the rate of in-hospital mortality was back then not lower than 19%. I can proudly say that today the in-hospital mortality due to acute myocardial infarction is 3–4% in our Center.

This is how the reperfusion era in treatment of patients with different forms of coronary heart disease has begun in Moscow, and, of course, all this became possible, first of all, thanks to the wise decisions and organizational activities conducted by Professor Vladimir Bourakovsky .

And in the end I wish to cite the words of a Dutch physician van Tulp who once said “Consumor aliis inserviendo”. This statement may be fully referred to Vladimir Bourakovsky, a person, who entirely devoted himself to the medicine and to serving the people of his country.

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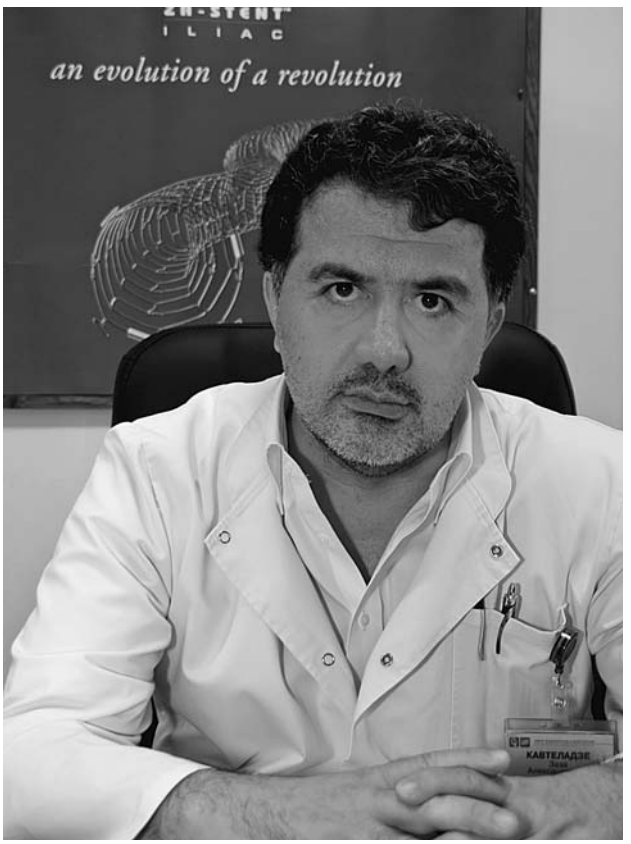
50th Anniversary of Dr. Zaza Kavteladze



Dr. Zaza Kavteladze turned 50 on December 6, 2012.

Dr. Kavteladze was born in Chiatura, Georgia. Having graduated from the university in 1987 he entered the clinical residency program and was referred to the Russian Scientific Center of Surgery to master the skills of arising specialty – interventional radiology.

Under the guidance of one of the pioneers of interventional radiology, academician I.Kh. Rabkin, Dr. Kavteladze mastered the techniques of diagnostis and treatment used in endovascular surgery. In 1990, he defended his thesis for the Candidate of Medical Sciences degree on laser angioplasty of peripheral arteries. His creative collaboration with talented engineer A.P. Korshok resulted in creation of authentic devices for endografting of vessels and hollow organs, removable vena cava filters, devices for the closure of intracardiac defects and temporary stents. All these inventions were patented in Russia and in Europe. Self-expandable stent, developed by Z.A. Kavteladze – the so-called ZA-stent – is registered in many countries worldwide and is manufactured by COOK Europe. Later on this stent has served as a base for the development of stent-graft used for endografting of the thoracic and abdominal aorta.

In 1993, Z.A. Kavteladze started working in the multi-field private clinic – Center of Endosurgery and Lithotripsy, and in 1995 became Head of the newly created Department of Interventional Cardiology and Angiology. Zaza Kavteladze has been one of the pioneers of percutaneous endografting using the linear stent graft, and 2 years later he also was the first to perform percutaneous bifurcated stent-grafting of abdominal aortic aneurysm. Achievements in endografting of aortic aneurysm were summarized in a doctoral thesis, which was defended in 2002. Dr. Kavteladze is a man of multiple scientific and practical interests. These include peripheral and coronary angioplasty, carotid stenting, angioplasty and stenting of coronary, peripheral, carotid, renal vessels, hollow organs, endovascular closure of cardiac septal defects, treatment of crural artery lesions in diabetic foot, embolization in pathological neoplasms, endovascular treatment of hysteromyoma. Over the recent years, Z.A. Kavteladze has patented several new methods of treatment in endovascular surgery with the use of authentic devices such as temporary (removable) stents, special introducer for antegrade femoral artery puncture, etc.

Scientific and educational activities of our hero of the day should be mentioned separately. Since 1995, seven international symposiums under the guidance and with direct participation of Zaza Kavteladze have been conducted in the Center of Endosurgery and Lithotripsy. In 1997, for the first time ever, the symposium with live-case demonstration form the cathlab was held in our country, and since then it has become a routine. Dozens of thematic seminars, conferences and meetings have been held by Dr. Kavteladze over these years. He is a professor of I.M. Sechenov First Moscow State University, thesis supervisor and counselor of the respondents.

In 2008, Z.A. Kavteladze was elected as a President of Russian Society of Interventional Cardioangiology, founded by the Corresponding Member of the Russian Academy of Sciences D.G. Ioseliani. In three years after 2008, the

Russian Scientific Society of Interventional Cardioangiologists conducted active scientific and educative work. Seminars on various aspects of interventional angiology and cardiology have been conducted, and the 4th Russian Congress of Interventional Cardioangiology was held in 2011.

For the several years, Z.A. Kavteladze has been a member of the steering committee of the largest domestic and international forums, such as PCR, TCT, C3, London Course on Endovascular Therapy, where he regularly appears as a speaker and moderator. Z.A. Kavteladze is an author of 120 articles, he wrote 8 chapters in the monographs.

Editorial Board of the International Journal of Interventional Cardioangiology congratulates the honoree, sincerely wishes him good health and further success in his scientific and practical activity.