ISSN 1727-818X

International Journal of Interventional Cardioangiology

№18
2009

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ISSN 1727-818X

INTERNATIONAL JOURNAL OF INTERVENTIONAL CARDIOANGIOLOGY

Quarterly Journal of the Russian Scientific Society of Interventional Cardioangiology

№ 18, 2009 г.

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

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Special gratitude to
George Gigineishvili,
doctor and artist, for the offered opportunity to put the photocopy of his painting
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ISSN 1727-818X
9 771727 818001

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Contents

Role of Clinical and Angiographic Factors of Using Bare-Metal and Drug-Eluting Stents in Real Clinical Practice in Patients with Unprotected Left Main Coronary Artery Stenosis

A.N. Samko[1], T.A. Batyraliev, I.V. Pershukov, I.V. Levitsky, I.A. Lazarev, E.V. Merkulov, O. Dogru, Yu.V. Pya, D.M. Ramazanov, L.V. Shul'zhenko, D.V. Fetzer, B.K. Kadyrov, F. Besnili

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INTRODUCTION

Lesion of the left main coronary artery (LCA) and its treatment represent an actual problem, and approaches to its solving are challenging so far. The presence of haemodynamically significant lesion of the LCA is prognostically unfavorable sign associated with high mortality if no revascularization is performed. This can be explained by the fact that a large portion of the myocardium, whose adequate perfusion is necessary for the normal heart performance, is supplied from the LCA system.

A. Gruentzig, a pioneer in angioplasty, was first to report percutaneous transluminal intervention in cases of stenosis of the LCA (1). He concluded that balloon angioplasty in the LCA is extremely difficult, while the mortality after the balloon dilatation of the LCA is unjustifiably high (1). Following the first attempts of catheter interventions in the LCA, in 1984 US National Heart, Lung and Blood Institute (NHLBI) has published the consensus, classifying lesions of the LCA as contraindication for percutaneous transluminal coronary angioplasty (PTCA) (2).

In 10 years after A. Gruentzig's angioplasties acceptable results of treatment of the LCA using balloon angioplasty were presented by O'Keefe et al. (3). Then, in 1997, ULTIMA (Unprotected Left Main Trunk Intervention Multicenter Assessment) Registry for percutaneous interventions in the unprotected LCA (balloon angioplasty, stents, direct atherectomy) registry was published. A conclusion was made that the only stenting and atherectomy contribute to significant improvement of the outcomes of percutaneous interventions in this pathology (4).

Encouraging results of percutaneous coronary interventions (PCI) with stenting of the LCA (5) have triggered conduction of new studies and a warranted revision of recommendations according to which PCI into the LCA was strictly inadvisable hitherto. Further progress of PCI used for the treatment of lesions of the unprotected LCA was related to the use of antiproliferative drug-eluting stents which decrease significantly the rate of subsequent re-stenosis and complications (6, 7).

However, the treatment of lesions of the unprotected LCA with implantation of bare metal stent (BMS) or drug-eluting stent (DES) is so far a complicated clinical problem, as the long-term outcome of PCI depends on a number of clinical and angiographic factors. Therefore, we decided to analyze results of implantation of BMS and DES into the unprotected LCA and to find out the reasons determining success and having impact on PCI complications.

MATERIAL AND METHODS

In the period from 2001 through 2005, 149 patients with lesions of the unprotected LCA were included in this study. Up to May, 2003, 63 patients undewent PCI with standard stents implanted into the LCA. From May, 2003, 86 patients with lesion of the unprotected main LCA underwent revascularization with implantation of drug-eluting stents into the LCA.

Their clinical characteristics are shown in Table 1.

Patients were hospitalized with stable exertional angina (II-IV functional class according to Canadian classification) or acute coronary syndrome (unstable angina with negative biochemical markers of myocardial damage). Hemodynamically significant stenosis (>50% of vessel diameter) in the LCA was revealed in these patients during coronary angiography. In some patients it was combined with other lesions of the coronary vessels.

Patients with history of coronary artery bypass grafting (and, therefore, with protected main LCA) were excluded from the study. Patients with lesion of the LCA within the first 7 days of MI with ST-elevation or MI without ST-elevation but with positive biochemical markers of myocardial damage ("troponin" MI) were excluded from the study as well. Moreover, patients with aspirin or clopidogrel intolerance were not included in study.

Angiographic exclusion criterion for this study was vessel reference diameter (VRD) at the site of stenosis below 3.0 mm or above 4.5 mm, vessel kink at the site of stenosis greater than 60°. Initial angiographic parameters of patients are shown in Table 2.

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Manuscript received on June 29, 2009.
Accepted for publication on July 28, 2009.

Table 1. Clinical characteristics of patients.

Parameter	Group of standard stents, N=63	ГGroup of drug-eluting stents, N=86	P
Males	47 (75%)	62 (72%)	NS
Smokers	31 (49%)	46 (54%)	NS
Arterial hypertension	42 (67%)	60 (70%)	NS
Diabetes mellitus	8 (13%)	14 (16%)	NS
Chronic kidney disease	6 (10%)	10 (12%)	NS
Hypercholesterolemia (> 5.2 mmol/L)	27 (43%)	33 (28%)	NS
Prior MI	11 (18%)	19 (22%)	NS

Table 2. Angiographic characteristics of patients.

Parameter	Group of standard stents, N=63	ГGroup of drug-eluting stents, N=86	P
Isolated stenosis of the LCA	30 (48%)	35 (41%)	NS
Distal (bifurcation) stenosis of the LCA with the LAD and/or the CxA involved	33 (52%)	51 (59%)	NS
Three-vessel lesion of coronary arteries (the LCA and the RCA)	8 (13%)	20 (23%)	NS
Length of stenosis of the LCA , mm	12±5	15±7	NS
Reference diameter of the affected segment of the LCA , mm	3.82±0.54	3,59±0,47	0.04
Range of reference diameters of the LCA in treated patients	3.0-4.5	3.0-4.0	-
Minimal diameter of the affected segment of the LCA , mm	0.91±0.67	0.89±0.61	NS
Percentage stenosis of the LCA	76±12%	75±11%	NS

TECHNIQUE OF PCI

Percutaneous coronary intervention in the LCA involved mandatory stent implantation in all treated patients. Stenting was performed after balloon predilatation of stenosis or by direct stenting if there was a possibility to place stent without prior dilatation of the narrowed segment. Stent implantation procedure lasted for 20-30 seconds under nominal pressure. Stent diameter to vessel reference diameter ratio of 1:1 was achieved with subsequent stent dilatations under pressure of 12 to 20 barometric atmospheres. Before 2003 standard bare stents, Multilink, BX Velocity, Ephesos were used for PCI. Starting from 2003 we are using sirolimus-eluting stents (SES – Cypher) and paclitaxel eluting stents (PES – Taxus).

Pharmacological support of stenting

Aspirin at a dose of 75 to 162 mg a day was administered to all patients from the moment of hospitalization. Patients received clopidogrel at a dose of 75 mg 2-4 days before stenting or at a dose of 300 mg 6 hours before PCI. After stenting patients were prescribed clopidogrel at a daily dose of 75 mg for 12 months.

During PCI all patients received unfractionated heparin (UFH) following the standard regimen, i.e. UFN was administered before the start of PCI intravenously under control of activated clotting time (ACT) at the dose of 70-100 IU/kg of body weight (target ACT = 300-350 sec); control of ACT continued every hour until the end of PCI, UFH was administered repeatedly at doses up to 40 IU/kg of body weight if necessary.

Follow-up

Analysis of PCI results included 2 endpoints.

The first endpoint – immediate outcomes (within 48 hours) and in-hospital outcomes (cumulative rate of the following events was estimated: death, occlusion of artery with subsequent MI, bleedings, necessity in urgent repeated intervention or CB surgery).

The second endpoint – combined clinical results at 6 and 12 months (incidence of death, MI, recurrence of angina, re-stenosis within 6 months and repeated revascularization within 1 year).

Statistics

Values are presented as mean ± standard deviation. Intergroup differences were assessed by means of analysis of variance or using nonparametric tests, while intragroup changes over time were assessed by analysis of variance for repeated measures or using nonparametric tests. “Statistica for Windows Release 6.0” (StatSoft Inc, USA) was used for analysis.

RESULTS

Diagnostic coronarography was performed prior to percutaneous intervention. Reference diameter at the site of lesion of the LCA was greater in the BMS

Table 3. Immediate results of stenting of the unprotected LCA.

Parameter	Group of standard stents, N=63	ГGroup of drug-eluting stents, N=86	P
Reference diameter of the affected segment of the LCA after PCI, mm	3,87±0,56	3,65±0,51	0.05
Minimal diameter of the affected segment of the LCA , mm	3,54±0,61	3,45±0,62	0.04
Percentage stenosis of the LCA	9±7%	5±4%	NS
Increase of stenosis diameter of the LCA , mm	2,63±0,75	2,56±0,71	NS
Final blood flow TIMI 3	61 (97%)	85 (99%)	NS
Final blood flow TIMI 2	2 (3%)	1 (1%)	NS
Complications of PCI	0	0	NS

group. In the DES group there were more bifurcation stenoses, in both groups (BMS and DES) bifurcation lesions were observed in more than a half of patients. Incidence of three-vessel lesion was higher in the DES group. In 84% of patients PCI was performed in 1-5 days after coronarography and in 16% of patients intervention was performed during the same procedure with coronarography. Bifurcation stenting was performed in the presence of distal (bifurcation) lesion of the LCA with the LAD and/or the CxA involved. There were no complications during PCI (Table 3).

Reference diameter of the affected segment and minimal diameter after stenting were greater in the BMS group, but percentage of residual stenosis was insignificantly lower in the DES group. The increase of vessel diameter was comparable in both groups (Fig.1 and Fig.2). The average length of the stented segment was 13 to 18 mm. The average increase of the artery lumen ranged from 2.56 mm in the DES group to 2.63 in the BMS group.

Within 2 day of observation following PCI, subacute thrombosis developed in 1 patient (2%) with the standard stent implanted. This patient had three-vessel coronary lesion and suffered from decompensated diabetes mellitus with high level of glycosilated hemoglobin; the patient refused the suggested coronary bypass grafting. Thrombosis resulted in extensive myocardial infarction with ST-elevation and death of the patient on the next day in spite of initiation of intra-aortic balloon pumping (IABP) and repeated PCI.

During follow-up period up to the time of discharge from hospital (Table 4) 1 patient from the DES group (1%) developed uncontrolled heart failure. This patient had a history of chronic kidney disease and creatinine clearance 38 ml/min/1.73m2. The patient also had IABP initiated and repeated catheterization. The stented segment was patent without signs of thrombosis. The patient died shortly after angiography in spite of active inotropic support.

Thus, in-hospital mortality was 1% in the DES group and 2% in the BMS group without significant differences and was related to baseline severe condition of the patients. The remaining patients had no PCI-related complications and were discharged.

After the discharge, during follow-up period up to 6 months, 8 patients in the BMS group (13%)

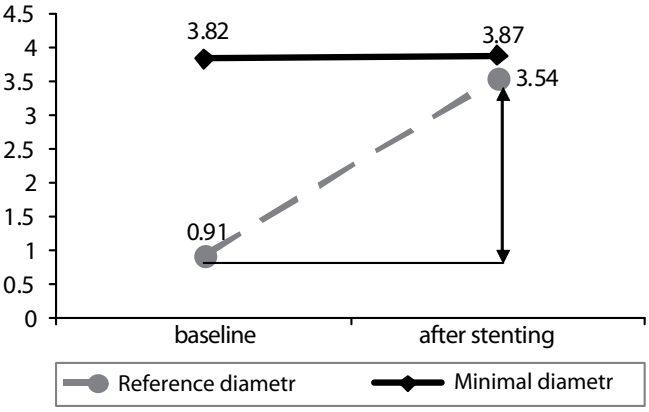

Figure 1. Changes in the diameter of the LCA after implantation of BMS.

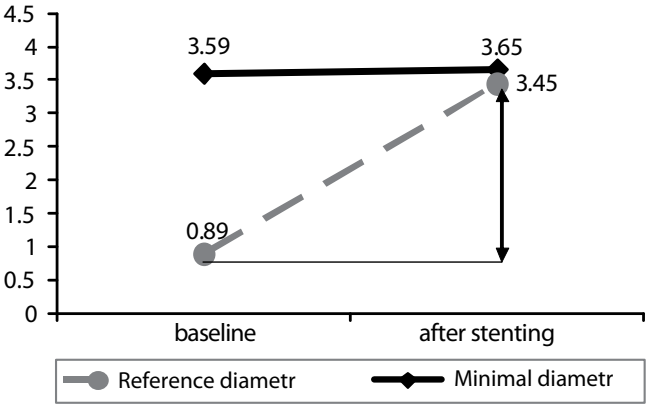

Figure 2. Changes in the diameter of the LCA after implantation of DES.

applied for medical care due to the recurrent angina (Table 5). Hemodynamically significant re-stenosis was revealed in them during the control coronary angiography. In the DES group during the first 6 months 6 patients (7%) complained of recurrent angina or acute coronary syndrome. Re-stenosis was also revealed in them at the control angiography. All patients with re-stenosis in the LCA underwent successful repeated revascularization. They underwent repeated PCI and, in case of three-vessel lesion, coronary bypass grafting.

Analysis of initial reference diameter of the LCA showed that the diameter was significantly smaller in patients returned with re-stenosis (Fig. 3). A separate analysis of the vessel reference diameter (VRD) demonstrated that in case of re-stenosis the average VRD was 0.49 mm lower in the BMS group and 0.44 mm lower in the DES group.

Table 4. In-hospital results of stenting of the unprotected LCA.

Parameter	Group of standard stents, N=63	ГGroup of drug-eluting stents, N=86	P
Discharged patients	62 (98%)	85 (99%)	NS
In-hospital MI	1 (2%)	0	NS
Acute heart failure	0	1 (1%)	NS
In-hospital mortality	1 (2%)	1 (1%)	NS

Table 5. Long-term results of stenting of the unprotected LCA.

Parameter	Group of standard stents, N=63	ГGroup of drug-eluting stents, N=86	P
Incidence of binary re-stenosis within 6 months	8 (13%)	6 (7%)	NS
Repeated revascularizations within 12 months	12 (19%)	8 (9%)	NS
Mortality within 12 months	2 (3%)	1 (1%)	NS

Review of the signs related to re-stenosis has shown (Table 6) that it developed more frequently in distal lesions in both groups, but the differences did not achieved the level of significance. Moreover, re-stenosis was found only in patients with diabetes mellitus and/or chronic kidney disease.

Within 12 months of observation repeated revascularizations were performed in 19% of patients in the BMS group and in 9% of patients in the DES group; these differences between groups did not achieved the level of significance (Table 5). One-year survival rate was high in both groups and even taking into consideration in-hospital mortality it was 97% in the BMS group and 99% in the DES group.

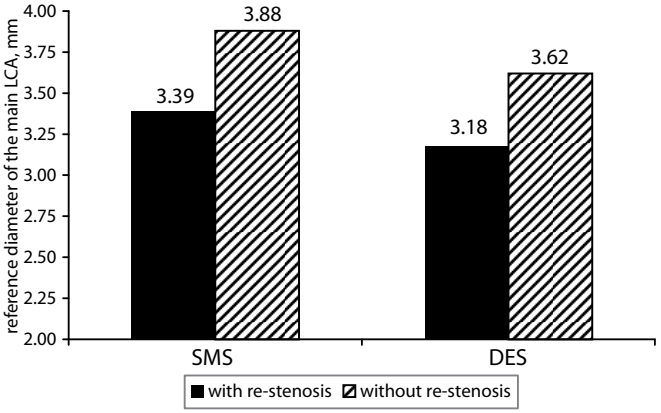

Figure. 3. Distribution of initial average VRD by groups corrected for re-stenosis.

DISCUSSION

The introduction of stents has improved the outcomes of PCI in the LCA, and DES permitted to reduce the number of subsequent revascularizations. Recent comparison of two DESs used for the treatment of lesions in the LCA demonstrated that both stents (Cypher and Taxus) had comparably low levels of cardiac complications and events within 1 year of observation (13.6% in the Taxus group and 15.8% in the Cypher group) (7). Two-year mortality was higher: 10.7% in the Taxus group and 8.7% in the Cypher group. The rate of re stenosis within 6 months after PCI was 16.0% in the Taxus group and 19.4% in the Cypher group.

In the other recent DISTAL study, Chen et al. evaluated the role of the distal bifurcation lesion of the LCA in the outcomes of implantation of drug-eluting stents (8). Among treated patients with lesions of the LCA, 164 had non-bifurcation stenosis, and 96 had stenosis with bifurcation involved. All patients were clinically monitored, and 86% of patients underwent control coronary angiography. During 2-year observation period it was revealed that as early as in 1 year there was a significant difference in the rate of major adverse cardiac events (MACE) between groups (9.1% MACE in the group with non-bifurcation stenoses versus 19,8% MACE in the group with bifurcation stenoses, p = 0.014). The same difference still

Table 6. Incidence of re-stenosis by groups and type of lesion.

	Re-stenosis within 6 months	
	Distal lesion of the LCA	Non-distal lesion of the LCA
BMS (n=63)	7 of 33	1 of 30
DES (n=86)	4 of 51	2 of 35

presented in 2 years (10.4% MACE in the group with non-bifurcation stenoses versus 25.0% in the group with bifurcation stenoses, p = 0.002). The main difference in incidence of MACE was due to the greater number of repeated revascularizations of the target vessel (RTV) in the bifurcation type of lesion (6.1% RTV in the non-bifurcation stenosis versus 16.7% RTV in bifurcation stenoses after 1 year of observation, p = 0.006, and 7.3% RTV versus 21.9% RTV, respectively, after 2 years of observation). In general, predictors of MACE were bifurcation lesion of the LCA (RR 3.42, 95% CI 1.34-5.61, p = 0.001), diabetes mellitus (RR 2.68, 95% CI 2.01-12.11, p = 0.015), and stent diameter in the LCA (RR 5.05, 95% CI 2.71-10.01, p = 0.03). Paradoxically, but the presence of three-vessel lesions (RR 0.83, 95% CI 0.27-0.96, p = 0.001) and incomplete revascularization (RR 0.15, 95% CI 0.11-0.35, p = 0.001) resulted in reduced incidence of MACE.

Our study demonstrated the superiority of DES compared to BMS in the treatment of the LCA lesions. Earlier we have already reviewed issues regarding the treatment of unprotected left main lesions, where the encouraging immediate and mid term results of the use of standard stents and drug-eluting stents were presented (9, 10, 11, 12). In this study immediate and in-hospital results of PCI were comparable in both groups, however, long-term results at 6 and 12 months were better in the DES group. Many parameters did not showed significant intergroup differences due to the small number of patients in the groups. However, all trends were in favour of drug-eluting stents. The rate of repeated revascularization within 1 year was 2-fold lower in the DES group (9% versus 19%). Angiographic reason for repeated revascularizations was re-stenosis, which developed more frequently in smaller vessels. This was true for both types of stents, BMS as well as DES. Repeated stenosis was observed in vessels with the reference diameter lesser than 3.5 mm, and when VRD was greater than 3.5 mm no re-stenosis was observed. Re-stenosis was more common with the bifurcation type of lesion, which was observed by other investigators as well (6, 7, 8).

Other diseases had impact on the incidence of long-term events as well: all patients with re-stenosis had diabetes mellitus and/or chronic kidney disease. Naturally, the presence of these diseases does not mean that patients with chronic kidney disease (CKD) and diabetes mellitus (DM) should avoid myocardial revascularization, but high risk of adverse events after any interventions (coronary bypass grafting and stent implantation) in such patients requires more intensive post-procedural management for reducing the risk.

CONCLUSION

Percutaneous coronary intervention with stenting of the LCA lesions is effective and safe during 1 year of observation. The use of drug-eluting stents improves long-term outcomes of PCI.

Other diseases had impact on incidence of long-term events as well: all patients with re-stenosis had diabetes mellitus and/or chronic kidney disease. Obviously, the presence of these diseases does not mean that patients with chronic kidney disease (CKD) and diabetes mellitus (DM) should avoid myocardial revascularization, but high risk of adverse events after any interventions (coronary bypass grafting and stent implantation) in such patients requires more intensive post-procedural care for reducing the risk.

CONCLUSIONS

1. Implantation of drug-eluting stents reduces the incidence of adverse long-term events and should be preferred during the intervention on the unprotected LCA.
2. Small reference diameter of the LCA (less than 3.5 mm) and bifurcation type of lesion increase the incidence of adverse long-term events after implantation of stent of any type.
3. History of diabetes mellitus and chronic kidney disease is a clinically unfavorable factor associated with the risk of adverse long-term events after PCI in the LCA .

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Surgical Approaches to Tumor in Left Atrial Myxomas

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According to autopsy data primary heart tumors are revealed in 0.0017-0.19% of cases (1). About half of them are myxomas. They are more common in women aged 35 55 years. In 80-90% of cases myxomas are localized in the left atrium (LA), significantly less frequently in the right atrium and very uncommonly – in the ventricles (2, 17, 22). LA myxomas in most cases originate from the region of fossa ovalis of the interatrial septum (IAS). LA myxomas must be surgically removed regardless of the presence or absence of complaints and neoplasm size. This is required due to high risk of endocarditis (3), main artery thrombosis (2,4) and sudden death (5).

The first successful resection of LA myxoma utilizing cardiopulmonary bypass was performed by Crafoord in 1954 (6). There is no unanimous opinion concerning optimal approaches to tumor, though tens of such surgeries have been performed in the majority of leading clinics, while worldwide experience comprises thousands cases. Some authors prefer the right atrial approach with the dissection of IAS (12), some prefer the parallel biatrial approach (16, 17, 22), and others use vertical biatrial approach with the dissection of IAS (14). Some surgeons use the upper, so called transplantation approach (15, 16). All these methods have their positive and negative aspects. Some of them provide better visualization but increase the risk of complications in the form of cardiac arrhythmia and bleeding. There are controversial opinions regarding the extent of resection. Some authors (16) adhere to removal of myxoma with its pedicle and nearby tissues, while others consider so called “shaving”, i.e. excision of myxoma from the pedicle, to be sufficient.

In this work we have analyzed the cumulative worldwide experience of researches in this area as well as present our own considerations regarding the extent of resection and approaches to LA myxoma with the account of its size and location.

Material and methods.

From May 2005 till now 9 resections of left atrial myxomas have been performed in Moscow City Center of Interventional Cardioangiology. No deaths were observed. Patients were aged from 50 to 69 (mean age 59.9±3.8 years).

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Manuscript received on May 15, 2009.
Accepted for publication on July 20, 2009

In most cases myxomas were the incidental findings during cardiological examination. The main complaints were palpitation, dizziness, sudden loss of balance sometimes related to the change of posture, and moderate dyspnea.

Diagnosis of LA myxoma was based on the data of transthoracic and transesophageal echocardiography. According to the ultrasound data myxoma size ranged from 1.5 to 5.0 cm in width and from 2.5 to 12.0 cm in length (mean size 3.5-5.2 cm). In 4 cases the tumor prolapse of variable extent into the left ventricle through the left atrioventricular ostium was observed (Fig. 1). In 8 cases myxoma originated from the interatrial septum (5 – in the region of the lymbus of fossa ovalis, 2 – in the fossa ovalis itself, 1 – in the inferior part of the interatrial septum) and in 1 case the postero-superior wall of the left atrium in the region of right inferior lobular vein served as a tumor basis.

The ultrasound data were completely confirmed during surgery. (Fig. 1)

SURGERY

All operations were performed under normothermic cardiopulmonary bypass with volumetric perfusion rate of 2.4-2.2 l/min with separate canulation of the vena cava and aorta. According to the protocol accepted in our Center, combined cold blood and crystalloid (Custodiol) cardioplegia was used for myocardial protection.

The approach to myxoma was chosen depending on its localization and size. We have used the following approaches:

1. Biatrial parallel to interatrial groove (IAG), with wide incision of the left and right atrium;
2. Approach through the right atrium – with the dissection of IAS;
3. Biatrial vertically in relation to the interatrial groove;
4. Approach through the right atrium with the dissection of the upper edge of IAS and minimal incision of the left atrium.

Parallel approach to the interatrial groove, incision of the left and right atrium (3 cases). After cardioplegia the right atrium is incised parallel to IAG at a length of approximately 5 6 cm. The upper edge of the incision is fixed by traction sutures.

Subsequently, the LA is incised in the same manner – parallel to the groove and over the right pulmonary vein ostia (5-6 cm). The LA is emptied of blood as carefully as possible and myxoma and its pedicle are found. Single traction sutures are applied on the

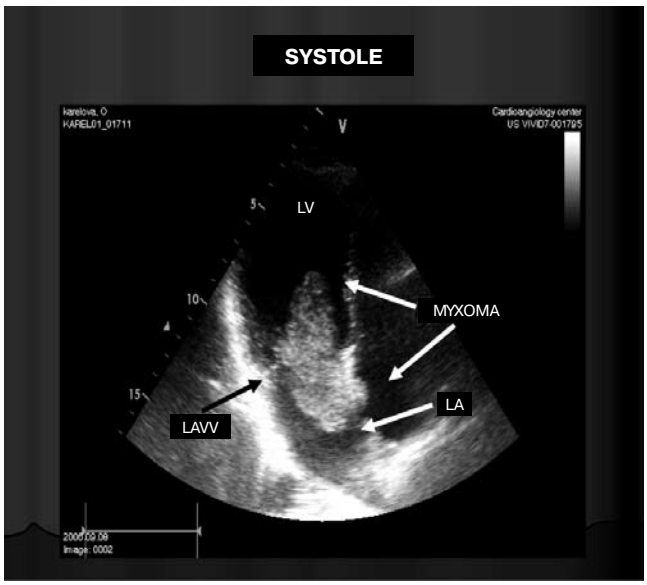
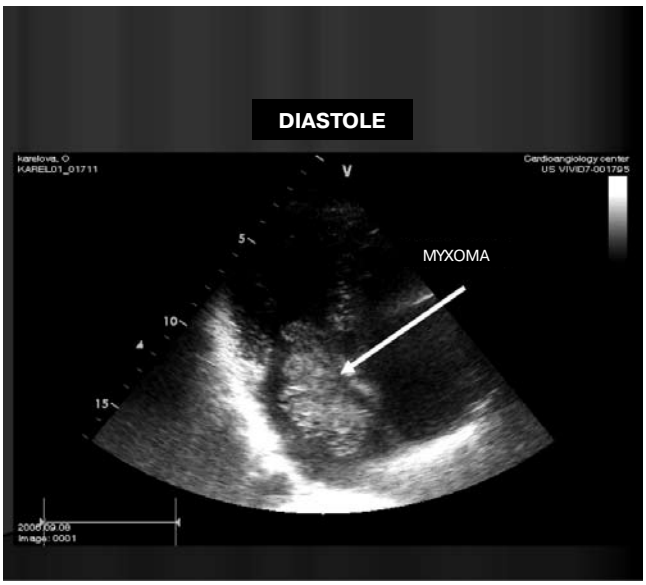


Figure 1.



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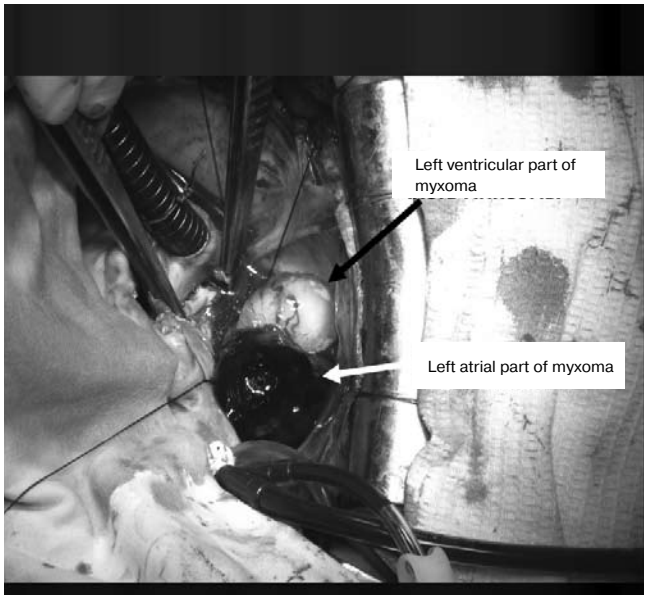

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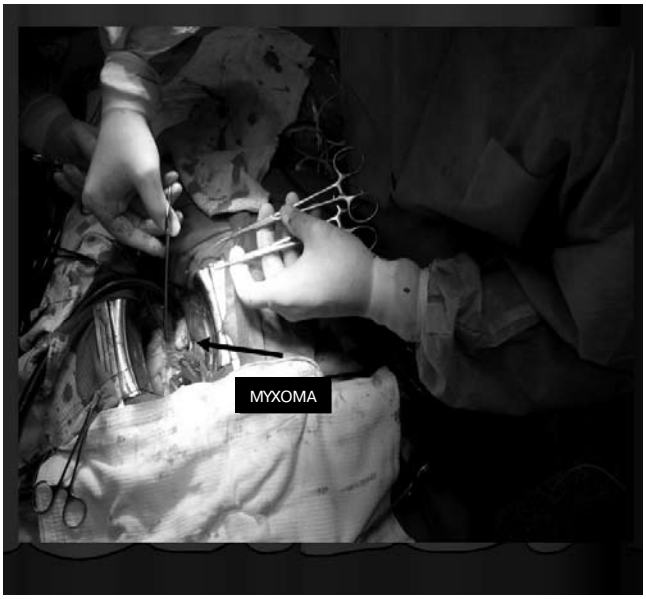

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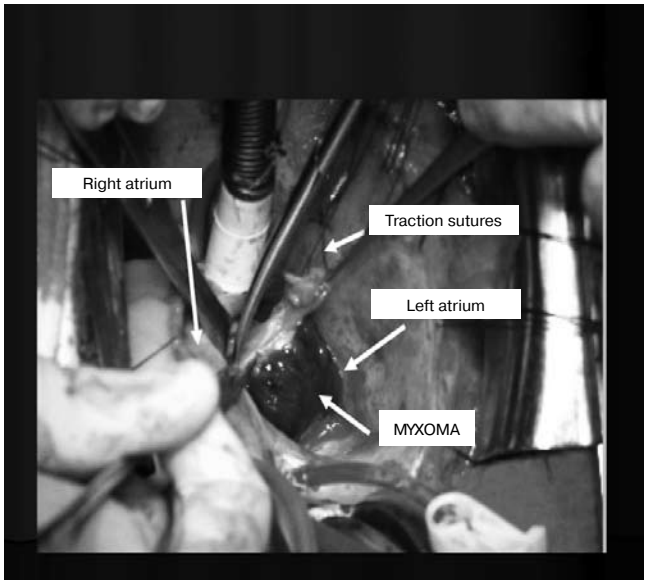

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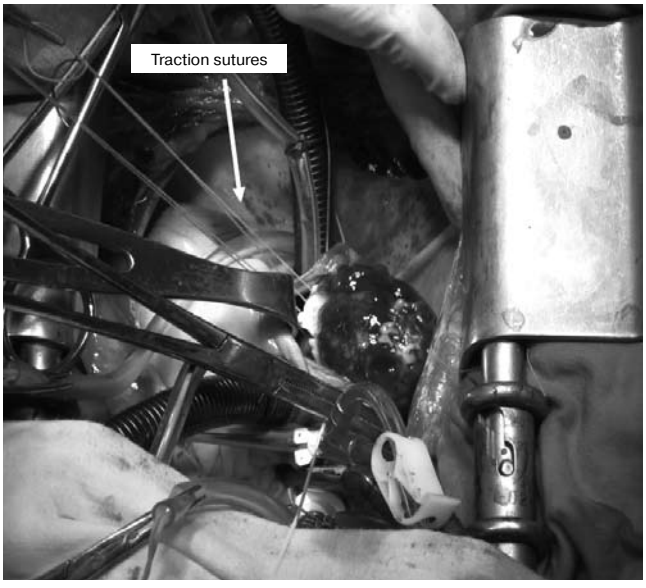

Figure 5.

tissues surrounding the myxoma pedicle and, then, IAS is incised with the scalpel and tumor is excised. Myxoma is removed through the incision in the left atrium. (Fig. 2).

The approach through the right atrium (1 case). The right atrium is incised from the base of the auricle towards the inferior vena cava (5-6 cm). The upper edge of incision is fixed by traction sutures. IAS is incised in the region of lymbus and is fixed by traction sutures. The IAS incision is extended sufficiently so that myxoma can be removed (Fig.3). Then myxoma is removed through the right auricle.

Biatrial approach using incision vertical to the interatrial groove (2 cases). The atrium is incised in the middle part vertically to the interatrial groove, the right atrium is incised up to the posterior wall of IAS projected between the right pulmonary veins. Then the left atrium is incised towards the incision in the right atrium between pulmonary arteries. The third stage is the incision of IAS itself towards myxoma basis. The edges of incision are fixed by traction sutures. Then tumor resection is performed (Fig.4).

The approach through the right atrium with the incision of the upper edge of IAS and minimal incision of the left atrium along the interatrial groove (3 cases). The right atrium is incised from the base of the auricle towards the inferior vena cava, and the left atrium is incised between the right pulmonary arteries for approximately 2 cm. After emptying the left atrium of blood, a surgeon defines the upper edge of myxoma using his finger or curved forcers. The IAS is incised on the instrument and traction sutures are applied on the side where the tumor is located. Then the base of myxoma is excised. In order to facilitate myxoma removal the superior part of IAS is incised towards atrium cupola. Then tumor is removed through the right auricle (Fig.5).

Myxoma excision. In all cases of myxoma location on IAS its basis was excised including at least 5 mm of surrounding tissue. Particular attention was given to prevention of Koch's triangle damage. In case of myxoma basis location on the left atrium wall it was cut subendocardially in order not to damage the left atrium wall and not to cause bleeding afterwards.

Repair of the iatrogenic IAS defect. In cases when the defect's size was over 1.5 cm it was repaired by autopericard patch plasty using single-row blanket suture (7 cases) (Fig. 6). The patches were prepared based on the data of heart ultrasound indicating the presence of wide myxoma base. In all other cases the defect was repaired using only single-row blanket suture (2 cases).

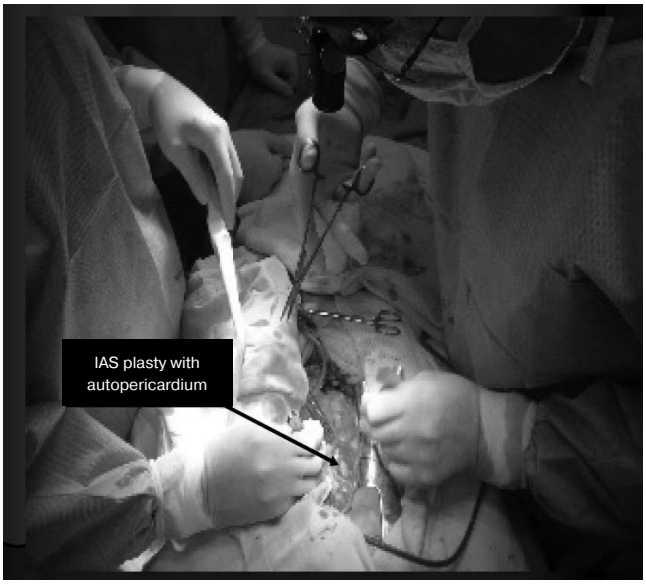

Figure 6.

RESULTS

No in-hospital deaths occurred. In early postoperative period cardiac arrhythmias in the form of nodal rhythm requiring temporary pacing were observed in 4 patients. Following appropriate drug therapy sinus rhythm recovered within 3-5 days in all patients. Different cardiac arrhythmias are seen after similar interventions in up to 50% of cases (10). There were no bleedings requiring resternotomy, as well as no other serious complications. All patients were discharged on day 12-14 in fair condition.

In the long-term follow-up (6-18 months), 8 patients were examined. According to EchoCG data there were no cases of myxoma recurrence or left-to-right shunt at the atrial level. All patients were active without any complaints.

DISCUSSION

Intracardiac myxomas are the most common cardiac neoplasms. In 75% of cases they originate from the region of fossa ovalis (2, 17). Approximately in 17% of cases the LA myxomas are localized in the region of the pulmonary veins (21). We have seen one female patient with such myxoma (11%).

These tumors originate from multipotential mesenchymal subendocardial cells (18). They are usually accidentally diagnosed. Sometimes patients present with moderate signs of heart failure, syncope, especially when changing posture, subfebrile fever of unknown cause, weight loss (10). Commonly seen laboratory abnormalities are as follows: increased ESR, monoclonal gammaglobulinaemia and microcytic anemia (19).

There is no unanimous opinion concerning the main aspects of surgery – the approach to the tumor and resection technique, though LA myxoma surgery has been developed for 55 years since the first successful surgery performed by Crafoord in 1954.

According to the literature data, in 38% of cases different types of biatrial approach are used, in 34% – the left atrial approach and in 28% – the right

atrial approach (12). The adherents of the left atrial approach (8, 9) believe that it ensures quite adequate conditions for tumor resection. But, in 35-85% of cases the authors performed only subendocardial tumor resection. The opponents of LA approach (9) believe that it is difficult and dangerous to remove large tumor through this approach. Furthermore, it is sometimes impossible to excise the edges of myxoma basis through this approach. The additional disadvantage is the impossibility to examine all four heart chambers. The last argument cannot currently be considered principal as modern EchoCG allows for topical diagnostics of myxomas of any location. Therefore, an intra-operative visualization of all chambers became not such an important issue. However, we share the opinion that this approach hampers manipulations on the tumor base, causing risk of embolism and, which is particularly important, makes the radical tumor resection impossible. With regard to the above mentioned we do not use this technique.

Although the right atrial transseptal approach is considered to be a minimally traumatic technique (10, 11), it is thought to be quite dangerous without transoesophageal Echo-guidance enabling the surgeon to visualize the basis of myxoma, especially if it has wide pedicle (9). Moreover, it is not always possible to remove large myxomas through this approach, and the lobular resection may be required (12). This risky manipulation may lead to embolism. Moreover, it is almost impossible to remove LA myxomas located in the region of pulmonary veins. We used this method in one case in myxoma measuring less than 3 cm in size. Using preoperative EchoCG we obtained precise data concerning the tumor basis localization and its size (less than 1,5 cm in diameter). We did not encountered any technical complications in any case and believe that this approach is quite acceptable and minimally traumatic for the treatment of small myxomas originating from IAS.

Biatrial vertical approach with the incision of IAS using Dubost technique (14), as well as upper "transplantation" approach proposed by Guiraudon (15), provide excellent visualization and allows to remove myxomas of any size (16). However they are traumatic and often lead to postoperative arrhythmia and may be associated with dangerous bleeding. We used the Dubost approach in 2 cases of large myxomas (10x5x4 cm and 6x3x3 cm in size) and consider this method to be the most appropriate for removal of tumors measuring more than 5 cm in diameter.

In 1973 Cooley was the first to use biatrial approach (20). He proposed to make a little incision in the left atrium for topical diagnostics of the base of myxoma. Other manipulations were performed through the right atrium and transseptally. However, this method does not also allow removing large myxomas of more than 5 cm in size. We used this approach in 3 cases and believe that it is a method of choice for removal myxomas of less than 5 cm in diameter.

In 3 cases we supplemented Cooley method with an incision of the upper muscular part of IAS up to atrium cupola if needed (approximately 1,5-2cm) with its subsequent suturing before repairing a iatrogenic IAS defect. This technique allowed us to enlarge the diameter of the orifice in IAS and to remove myxomas with a diameter of more than 5 cm. We believe the advantages of this method to be as follows: good visualization of a tumor with no risk of its damage, no necessity to extend the incision towards the region adjacent to Koch's triangle and, as a possible consequence, development of AV block. With the use of our approach it is possible to remove the majority of LA myxomas without increasing the risk of postoperative bleeding or cardiac arrhythmia.

A simple excision technique ("shaving") leads to delayed relapses in 5-12% (8, 10, 12). It is particularly common in cases of familial myxomas. Thus, taking into account the impossibility of tracing the genetics in all patients, it may be supposed that myxoma pedicle incision with IAS and adjacent demarcation zone of approximately 5 mm in width should be a method of choice.

In what concerns the method of iatrogenic IAS defect closure we share the opinion of authors (12) that defects of less than 15 mm in size can be closed using simple blanket suture, and larger defects – using an autopericardial patch.

Thus, surgical treatment of LA myxoma is the only and mandatory treatment method for this disease. Currently, heart ultrasound examination allows us to obtain comprehensive information on location and anatomy of a tumor. Using these data we can precisely plan the extent of intervention. Modern methods of anesthesia, cardiopulmonary bypass and myocardial protection along with appropriate surgical strategy contribute to performance of these operations with minimal risk. The surgical approach to a tumor must be defined depending on tumor location and sizes. Proposed biatrial approach along the interatrial groove with a little incision in the left atrium and incision of the upper edge of IAS allows for radical excision of the majority of LA myxomas with minimal risk of preoperative and post-operative complications.

CONCLUSIONS

1. With appropriate support of surgery and adequate surgical tactics LA myxoma can be excised without significant complications.
2. The rough manipulations on the heart and myxoma itself should be avoided both before cardiopulmonary bypass and during the main step of surgery.
3. In order to prevent myxoma dislocation its pedicle with surrounding tissues must be fixed by traction suture as soon as possible;
4. It is easier to remove giant (more than 7 mm in diameter) myxomas through biatrial approach.
5. The majority of myxomas may be excised using modified parallel biatrial approach with minimal

incision of the left atrium and additional incision of the upper part of IAS.
6. It is expedient to remove myxoma with surrounding tissues (5 mm IAS).
7. Iatrogenic IAS defects with a diameter of more than 15 mm should be closed using autopericardial patch.

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Endovascular Treatment of Renal Artery Stenosis in High-Risk Patients

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This work presents immediate and mid-term results of renal artery stenting in 76 patients at high risk of serious complications following endovascular procedures. These include patients with renal artery stenosis in single kidney, patients with chronic renal diseases, diabetes mellitus, those with procedures performed concurrently on both renal arteries etc. The study demonstrated that in overwhelming majority of patients (75%) the procedure resulted in significant antihypertensive effect, which was observed in mid-term follow-up in 67% of patients. Immediately after the procedure a moderate impairment of renal function was observed in approximately 20% of patients which then recovered in all of them within the first week. In no case dialysis was required. In the long-term follow-up the recurrence of arterial hypertension was observed in approximately 33% of patients; however, it required less drug therapy compared to that before stenting. Renal function impairment was observed in approximately 5% of patients but did not require dialysis in any case.

Keywords: atherosclerosis, renal arteries, angioplasty.

Arterial hypertension (AH) is a serious medical and social problem today, and its contribution in mortality and disability is still growing despite particular attention paid to this issue by the healthcare managers and practitioners. In the morbidity structure of AH, vasorenal disease accounts for 4% of cases (1). Vasorenal hypertension is diagnosed more often in patients with severe or rapidly progressive forms of AH, relatively refractory to drug therapy, with the rate reaching 15%, particularly in patients older than 40 years. In elderly patients with advanced diffuse atherosclerosis the probability of atherosclerotic renal artery stenosis can exceed 50% (2, 3). In such cases the involvement of other vascular basins are often observed according to data from other studies (4, 5). Alcasar et al. reported that renal artery disease is most commonly associated with the impairment of peripheral (67.9%) and coronary (45%) arteries. It is important to note that 11.5% of patients with renal artery stenosis suffer from complicated arterial atherosclerosis of all three localizations (coronary, cerebrovascular and peripheral). Therefore, patients with renal hypertension caused by renal artery stenosis are quite often at high risk. Patients with uncontrolled AH, renal failure, involvement of both kidneys (bilateral lesion), renal arteries' lesion in single kidney, and concomitant nephrogenic pathology also should be included in this category.

Stenting is known to be an effective method for the management of vasorenal hypertension due to renal artery stenosis. In 2005, American Heart Association (AHA) and American College of Cardiology (ACC) published joint recommendations in which the modern approaches to endovascular treatment of renal artery stenosis and occlusive disease are outlined. These recommendations explain in detail the indications for revascularization procedures in the treatment of renal artery diseases. These indications are summarized in Diagram 1.

The diagram demonstrates that, until recently, all "symptomatic" stenoses, including stenoses in high-risk patients were indications for renal revascularization. In patients with significant renal artery stenotic changes and AH poorly managed with medication, endovascular renal reperfusion is not a subject of considerable discussion provided that there are no concomitant diseases. At the same time the choice of method is still a subject for discussion in other subsets of patients, having such concomitant diseases as severe renal failure caused by parenchymatous pathology. A randomized ASTRAL (Angioplasty and Stent for Renal Artery Lesions) trial (completed in 2008) evaluating the efficacy of endovascular treatment compared to conservative drug therapy in patients with renal artery stenosis and renal failure (serum creatinine of approximately 2 mg/dl) did not reveal any superiority of renal revascularization versus optimal drug therapy (6, 7).

Nevertheless, the authors did not exclude a possibility of performing renal arteries revascularization in patients with acute renal or heart failure.

Revascularization is primarily indicated in patients with refractory and poorly controlled hypertension. Arterial hypertension inadequately controlled with medication, increases the risk of cardiovascular complications, therefore, angioplasty (with or without stenting) should be performed in case of failed drug therapy. Preliminary data from the CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) trial that will be completed in 2010, also should be considered ambiguous (8, 9). The question whether endovascular therapy in combination with drug therapy compared to drug therapy alone reduces the rate of cardiovascular events in patients

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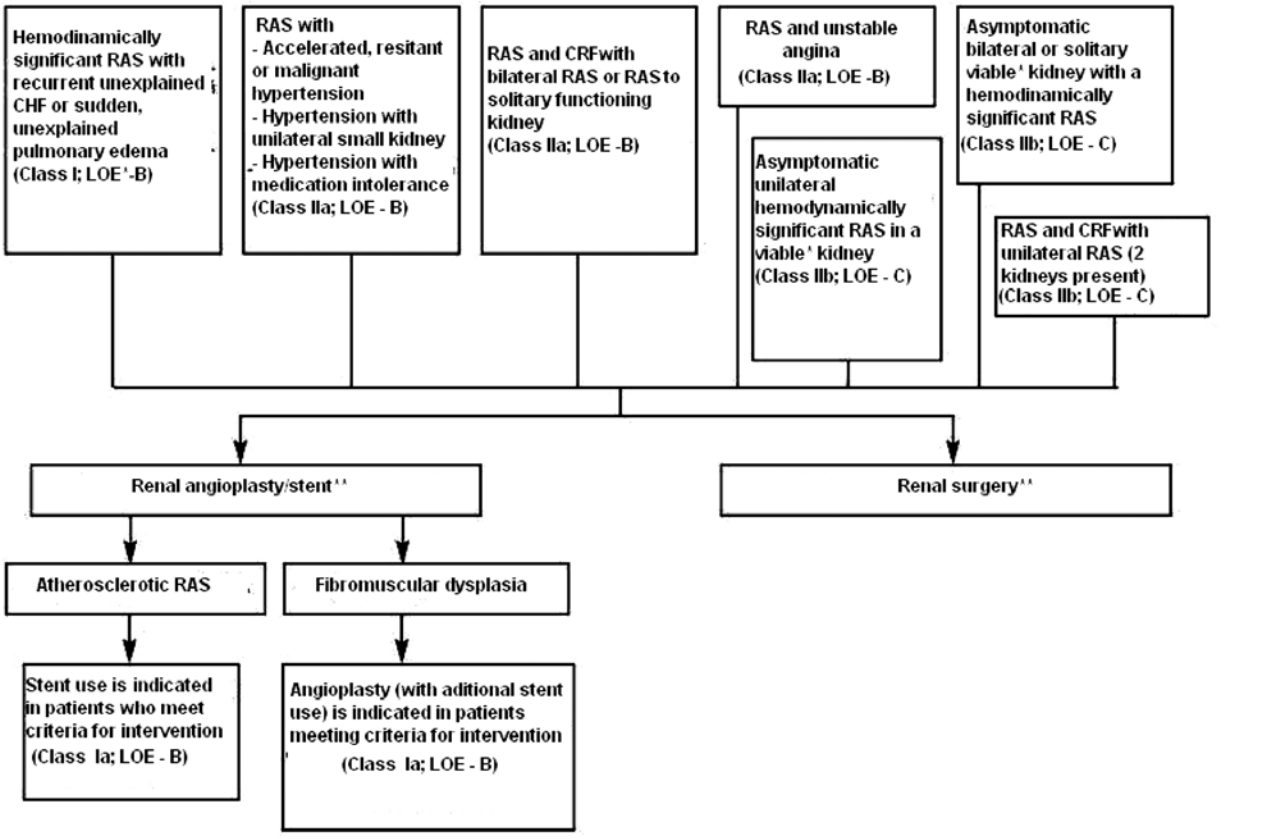
Accepted for publication on July 20, 2009.

Diagram1. Modern indications for renal artery revascularization and assessment of their evidence-based reasoning (Guidelines of AHA/ACC 2005).



Note: Class I benefit >>> risk; Class IIa: benefit >> risk; Class IIb: benefit > risk. LOE -level of evidence; B - treatment is useful/effective Evidence derived from a single randomized trial; C - treatment is useful/effective. Evidence derived from consensus opinion of experts; ' kidney measured >7 cm in size; ' ' It is recognized that renal artery surgery has proven efficacy in RAS due to atherosclerosis and fibromuscular displasia. Currently, however, its role is often reserved for patients in whom invasive percutaneous interventions are not feasible

Table 1. Vascular complications in the stenting group versus drug therapy during 1 year of follow-up.

Results	Revascularization (N = 369)	Drug therapy (N = 380)	P
Myocardial infarction	6%	8%	0.3
Hospitalization due to angina	7%	8%	0.5
Hospitalization due to heart failure	12%	14%	0.3
Stroke	5%	5%	0.8
CABG or PTCA	2%	3%	0.6
N of events/N of patients	109 / 83	132 / 100	0.2

CABG – coronary artery bypass grafting

PTCA – percutaneous transluminal coronary angioplasty

with renal artery stenosis could not be answered positively. Nevertheless, the authors believe that renal revascularization should be performed in case of AH poorly managed with medication.

Thus, to date the majority of researchers support the tactics of endovascular treatment in patients with renal artery stenosis and uncontrolled AH, including those with acute renal and heart failure. At the same time, many issues concerning indications for endovascular procedures still remain incompletely clear. In what case the drug therapy for vasorenal hypertension can be deemed ineffective and endovascular reperfusion should be considered? What grade of renal failure should be deemed an indication for renal artery angioplasty as it is known that renal impairment caused by renal artery stenosis may be transitory due to atheroembolism originated from unstable atherogenous plaque (10). There is also a latent stage of renal failure when random creatinine values remain within normal limits, but in case of systematic follow-up they may increase significantly especially under the influence of certain factors (medications, intercurrent infections, hypovolemia) precipitating manifestation of renal failure. It should be noted that renal failure in elderly patients may be caused not only by chronic hypoperfusion of renal tissue due to bilateral renal artery stenosis, but also by combination of renal ischemia with analgetic or urate tubu-

lointerstitial nephritis, chronic pyelonephritis, diabetic nephropathy and age-specific changes in renal tissues (11). Therefore, these questions should be subject to additional investigation and clarification.

Thus, we consider reasonable to share our experience of endovascular treatment of the renal artery in high-risk patients of different categories. Our experience includes endovascular renal artery interventions in 76 high-risk patients.

Table 2. Nature and incidence of risk factors in the studied group of patients.

Concomitant pathology	Number of patients, n (%)
Stenotic lesion of unique kidney	1(1.3%)
Bilateral renal artery stenoses	28 (36.8%)
Renal failure	28 (36.8%)
Chronic renal diseases (pyelonephritis, urolithiasis)	15 (21.1%)
Nephrosclerosis (based on RI of segmental arteries)/ marked nephrosclerosis	42 (55.3%)/ 8 (10.5%)
Persistent AH (3 and more antihypertensive agents)	20 (26.3%)
Diabetes mellitus	12 (15.7%)
CHD	44 (57.9%)
Stenotic atherosclerosis of brachiocephalic arteries	16 (34.2%)
Leriche syndrome	23 (30.3%)

All patients had AH, in 26.3% of cases it was relatively refractory to drug therapy.

Renal function deterioration was observed in 28 patients (36.8%), in 2 cases it was significant (serum creatinine up to 300 μm/l), in other cases it was moderate (serum creatinine ranging from 131 to 152 μmol/l).

It should be noted that initial renal function impairment with mean elevation of serum creatinine up to 136±21 μmol/l was revealed in 50% of patients with bilateral renal artery disease.

Prior to endovascular intervention the average degree of renal artery stenosis in the studied patients was 77±9.2%. Angiographic picture of renal artery lesions suggested their atherosclerotic origin.

Before endovascular intervention the patients underwent the following examinations: kidney ultrasound examination with evaluation of renal arterial blood flow, as well as intrarenal blood flow with determination of peripheral resistance index, which is an ultrasound criterion of nephrosclerosis; 24-hour blood pressure monitoring; determination of urea and creatinine levels before and immediately after the procedure and before discharge; diagnostic angiography.

Follow-up examination, including angiography, was performed in 43 patients at 8.3±2.6 months (mean). In 15 cases the follow-up period was over 2 years.

STUDY RESULTS AND DISCUSSION

Following examination 87 renal artery stenting procedures were performed in 76 patients. The mean volume of contrast media injected during procedure was 365±167 ml. The low-osmolarity contrast agent was used in all cases.

All patients were followed in the intensive care unit for 4-5 hours after endovascular renal artery angioplasty. Continuous BP and ECG monitoring was performed, and blood coagulation parameters were controlled as well. In order to prevent stent thrombosis the patients received clopidogrel (plavix) at a daily dose of 75 mg for 1 month after the procedure.

An optimal angiographic result of the angioplasty was obtained In 75 cases (98.7%). One procedure (1.3%) was complicated by occlusive dissection of the renal artery requiring surgical intervention.

Immediately after stenting a antihypertensive effect was noted in all patients. In 75% of cases the effect was marked, in 25% there was a trend towards decrease due to reduced values of maximal BP elevation with the “working” blood pressure remaining at the previous level.

After endovascular intervention renal function monitoring was performed. In 16 patients (21%) the transient renal function impairment or contrast-induced nephropathy (CIN) was reported immediately after the procedure with subsequent normalization within a week.

Within 6-12 months after the procedure the state of 49 stented renal arteries was evaluated in 43 patients. Mean duration of follow-up was 7.9±2.8 months. In-stent stenosis was revealed in 8 cases (16.3%) which is consistent with the literature data suggesting the rate of in-stent stenosis ranging from 11 to 23% (12, 13). In all cases of in-stent stenosis the endovascular correction (angioplasty or stenting) was performed with good effect.

Follow-up examination revealed the preservation of initial antihypertensive effect in 67% of cases; in 33% of cases recurrence of hypertension was revealed. However, a careful analysis demonstrated significant decrease in the number of antihypertensive agents taken (from 2.5±0.6 to 1.7±0.9, p=0.0007) and improved efficacy of antihypertensive therapy (57%) compared to baseline (10.7%), including patients with recurrent AH.

Among repeatedly examined patients, the renal function stabilized by this time in 32 (74.4%) patients, improved in 9 patients (20.9%) with normalization in 4 out of these patients, and in 2 (4.7%) patients the renal function deteriorated.

Particular attention was paid to the patients with CIN. Six of them underwent follow-up examination. It was found that renal function improved in 5 (83.3%) patients compared to baseline. In one case renal function deteriorated. It should be noted that this deterioration revealed in a patient with concomitant renal pathology (chronic pyelonephritis). It should be especially noted that no significant renal function worsening was revealed in any case of in-stent

stenosis. In these patients both baseline and control values of serum creatinine did not exceed normal limits. These observations suggest that the main cause of renal function worsening in renal artery stenosis consists in repeated atheroembolism from the plaque and not in the ischemia as such (10).

We investigated renal function dependence on the degree of atherosclerosis. The highest baseline creatinine values were observed in patients with marked nephrosclerosis (p=0.001). Follow-up examinations in these patients revealed decrease in serum creatinine after stenting, but no normalization was observed. In patients without nephrosclerosis or with moderate process both baseline and control values of serum creatinine did not exceed normal limits.

Fifteen patients were followed-up over longer period (3.43±1.59 years), 6 out of them underwent balloon angioplasty due to previously diagnosed in-stent stenosis. All followed patients with plasty of in-stent stenosis had good results of previous procedures. Primary in-stent stenosis was found in 2 cases (14.3%). Antihypertensive effect was preserved in 67% of cases, no renal function worsening was observed.

CONCLUSION

Thus, on the base of our results we can state that endovascular renal reperfusion is a safe and effective treatment method in the majority of patients with renal artery disease and high risk of complications. However, the feasibility of endovascular intervention in this category of patients should be considered individually in each particular case taking into account all characteristics of a given patient.

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Anatoly Malashenkov

On September 16, 2009 the eminent Russian scientist and cardiac surgeon, corresponding member of Russian Academy of Medical Sciences, honored worker of science, professor, laureate of State prizes of USSR and RF Anatoly Malashenkov accomplished 70 years. Together with such personalities as Vladimir Bourakovsky, Victor Saveliev, Grigory Tsoukerman, Anatoly Pokrovsky, Vladimir Podzolkov, Vladimir Alexi-Meskishvili, Mikhail Semenovsky, Vladimir Rabotnikov, Vladimir Ilyin, and others, he belongs to a distinguished and famous galaxy of cardiac surgeons of "Bakulev school"

A brilliant surgeon possessing a virtuosic technique, Anatoly Malashenkov has performed thousands of complicated heart operations. Many of these operations were done for the first time in Russia and served as a base for further successful development of national cardiac surgery. Professor Anatoly Malashenkov is rightfully considered a leader in the surgery of acquired heart diseases and reconstructive surgery of the aneurysms of the ascending aorta and the aortic arch.

Beside being a notable surgeon A. Malashenkov is a magnificent, remarkably literate clinician, knowing all the ins and outs of cardiovascular diagnostics. Due to his attention and empathy to patients he earned a well-merited respect and fame among patients and colleagues.

Professor Malashenkov attach a great value to research work. He developed the basics of the problem of myocardium protection during open-heart surgery; the tactics of surgical treatment of acute ascending aortic dissection; the problems of multivalvular replacement; thrilling aspects of surgical treatment of heart tumors. He is the author and co-author of hundreds of scientific papers and a number of monographs. Scientific research in the field of cardiac surgery brought to Anatoly Malashenkov several State prizes of USSR and Russia. He also was awarded the Order of Honor.

Anatoly Malashenkov gives a great attention to the formation of young specialists, and many leading Russian cardiac surgeons consider him as their teacher and are proud of this. Thirteen Doctor and Candidate theses were prepared and defended under his personal guidance. He is the Member of many International and Russian scientific societies and councils.

Anatoly Malashenkov is known for his incredible modesty, honesty, friendliness and kind-heartedness. He is loved and respected by all those who know him.

The Editorial board of the Journal wishes Professor Anatoly Malashenkov to enjoy good health, happiness and great creative successes.