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Efficacy of Drug-Eluting Stent Use for Simple and Complex Correction of Stenotic Lesions of the Left Main Coronary Artery Bifurcation

B.E. Shakhov, E.V. Chebotar, A.V. Kazakovtsev, E.A. Kuzmenko, A.V. Zakrevsky, O.V. Britvina[1], E.B. Shakhova
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INTRODUCTION

Approaches to the treatment of patients with the lesions of the left main coronary artery (LMCA) bifurcation are still disputable. Many authors consider bypass surgery as the treatment of choice for the lesions of LMCA. In their opinion, percutaneous coronary intervention (PCI) of LMCA lesions should be used only in patients who are not eligible for surgical treatment for some reasons or refuse it (1,5). Usually they refer to increased risk of interventions in the left main area as well as the high rate and the danger of restenosis after intervention (2). Others believe that the use of interventional methods for the correction of the left main stenosis is quite reasonable and at least as effective as the bypass surgery (3). Ongoing studies continuously expand available knowledge and ideas about the risk and the effectiveness of surgical and interventional treatment in this population of patients. The data obtained in these studies allow to define patients with LMCA lesions in whom PCI is be at least as effective as bypass surgery (16). When choosing the method of revascularization for this the patient with LMCA disease the localization of the lesion in the left main is a key point. Lesions of LMCA involving the distal segment are the most complex and risky for PCI and to date no ideal stenting technique is elaborated for this localization (4, 5, 8). Bifurcation lesion increases not only the risk of the intervention itself but it also is related to worse long-term prognosis. Restenosis after stenting of LMCA is known to develop less frequently in the ostium and middle segment of the left main and significantly more often in its distal segment and ostia of the circumflex (CxA) and the left anterior descending artery (LAD) (5, 12, 13, 14). Taking into consideration that restenoses in this area are often asymptomatic although extremely dangerous, the problem of fighting the restenoses while correcting the bifurcation of LMCA is really crucial. In the era of bare metal stents the mortality caused by restenoses of the LMCA reached 20% by the end of the first year (2). Introduction of the drug-eluting stents into the clinical practice holds out a hope of improving long-term outcomes of endovascular correction of lesions located at the bifurcation of the LMCA. The problem of stent choice (DES or bare metal) for the correction of bifurcation lesions of the LMCA is one of the most important issues which is to be solved before interventional correction of main LCA bifurcation is attempted.

The next and at least equally important issue in LMCA correction is the choice of correction technique. The use of complex techniques with two stents implantation and the formation of double- or triple-layer coverage of the arterial wall ("culotte", "crush") is known to give good angiographic and immediate clinical results. However, according to several authors, long-time results of these techniques use for the correction of "non-left main" bifurcations have no advantages over the results of "one-stent" techniques (9,10,11). Recent meta-analysis of six randomized studies comparing the efficacy of "two stents" and "one-stent" correction of bifurcation lesions suggest that stenting of both main and side branches ("complex" correction) is associated with an increased risk of MI and, probably, with an increased risk of stent thrombosis (18). On the other hand, correction of left main bifurcation with one stent does not always lead to good angiographic results and the intervention itself is very risky. The "two-stents" techniques which are not accompanied by "duplication" or "triplication" of stent coverage of the arterial wall – V-, "kissing"-, Y- and T-stenting – represent a separate problem. The use of these techniques allows for complete "coverage" of the affected segment of bifurcation without stents overlapping. The "two-stents" techniques vary in difficulties of performance and the degree of risk, and these are the characteristics which must be first considered while correcting the left main bifurcation lesions. All these considerations explain our interest to the use of "one stent" and some "two-stents" techniques for the correction of LMCA bifurcation lesions.

PURPOSE OF THE STUDY

To compare the results of "one-stent" and "two-stents" endovascular interventions with DES and bare metal stents implantation in patients with bifurcation lesions of LMCA.

MATERIAL AND METHODS

Results of endovascular interventions in 58 patients (44 males and 14 females) aged 39-86 years (mean

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age 56.4±1.2 years) with atherosclerotic lesion of the LMCA bifurcation were analyzed. 32 patients were admitted with clinical signs of chronic stable angina of III-IV functional class, 8 patients had II functional class according to CCS. 18 patients (31.0%) were admitted to the hospital with acute coronary syndrome (ACS). 30 patients (51.7%) had history of acute myocardial infarction (AMI). 39 patients (67.2%) were hypertensive and 4 had diabetes mellitus (6.9%). Left ventricular ejection fraction (LVEF) varied from 33 to 69% (mean value 53.8±1.0%). 11 patients (19.0%) had low ejection fraction.

The patients were divided into 2 groups. The first group comprised 23 patients who underwent correction of LMCA bifurcation with drug-eluting stent. The second group consisted of 35 patients in whom bare metal stents were implanted. There were no significant differences between main clinical characteristics of patients in groups I and II (Table 1).

The evaluation of coronary angiography showed that 29 patients had bifurcation lesion of the LMCA only, and in 21 patients lesion of LMCA bifurcation was associated with other coromary lesions. 6 patients had lesions of two coronary arteries, and 2 patients had occlusion of the right coronary artery in addition to bifurcation lesion of the LMCA. Comparison of coronary lesions distribution in groups I and II patients is shown in Table 2. There was no significant difference between first and second groups of patients in terms of coronary lesion severity.

Type of bifurcation lesion of the LMCA was determined according to classification of A. Medina (6). Type “1.1.1” was diagnosed in 12 patients. “1.1.0” – in 3 patients, “1.0.1” – in 3 patients, “1.0.0” – in 1 patient, “0.1.1” – in 6 patients, “0.1.0” – in 23 patients and “0.0.1” – in 10 patients. The incidence of different types of bifurcation lesions in groups I and II is shown in Table 3.

Endovascular intervention was performed via femoral approach in 56 patients and with radial approach – in 2 patients. Correction of the LMCA lesion with 1 stent was performed in 39 patients, with 2 stents – in 17 patients and with 3 stents – in 2 patients. For “two-stents” correction V- or “kissing”-stenting techniques were used in 15 cases and “crush”-stenting was performed in 2 cases. Y-stenting with implantation of 3 stents was performed in 2 patients.

Final formation of bifurcation using “kissing balloon” technique was used in 18 cases of “two-” or “three-stents” correction and in 15 cases of “one-stent” correction. Additional stenting of other coronary arteries was performed in 20 (34.5%) patients.

Intra-aortic balloon pump was used during endovascular interventions in 6 patients. Details of endovascular interventions in patients from different groups are shown in the Table 4.

Control clinical examination including coronary angiography (6 - 46 months) was performed in remote period for 50 patients (86.2%): 22 patients from group I and 28 patients from group II.

Table 1. Clinical characteristics of patients in groups I and II.

Parameter	Group I (n=23)	Group II (n=35)	P
Mean age	57.5±2.1	55.6±1.5	0.453
Males	20 (87.0%)	24 (68.6%)	0.198
Arterial hypertension	14 (60.9%)	25 (71.4%)	0.581
Diabetes	2 (8.7%)	2 (5.7%)	0.927
History of AMI	13 (56.5%)	17 (48.6%)	0.746
History of CABG	3 (13.0%)	5 (14.3%)	0.799
Previous PCI	8 (34.8%)	4 (11.4%)	0.069
Angina: Calss II Class III-IV ACS without ST-elevation	 4 (17.4%) 15 (65.2%) 4 (17.4%)	 4 (11.4%) 17 (48.6%) 14 (40.0%)	 0.799 0.329 0.126
Mean EF (%)	54.9±1.4	53.0±1.3	0.338
EF < 50% (%)	5 (21.7%)	6 (17.1%)	0.738

Table 2. Distribution of coronary lesions in patients from groups I and II.

Distribution of coronary lesions	Group I (n=23)	Group II (n=35)	P
Isolated lesion of the left main bifurcation	10	19	0.591
Lesion of of the left main bifurcation + lesion of 1 coronary artery	8	13	0.923
Lesion of of the left main bifurcation + lesions of 2 coronary arteries	4	2	0.323
Lesion of the left main bifurcation + occlusion of RCA	1	1	0.666

Table 3. Types of bifurcation lesions of the left main in patients from groups I and II.

Type of lesion (A. Medina)	Group I (n=23)	Group II (n=35)	P
1.1.1	7	5	0.249
1.1.0	1	2	0.707
1.0.1	2	1	0.556
1.0.0	0	1	0.831
0.1.1	3	3	0.915
0.1.0	8	15	0.733
0.0.1	2	8	0.298

Table 4. Characteristics of PCI in patients from groups I and II.

PCI features	Group I (n=23)	Group II (n=35)	P
Predilatation of LMCA	17	24	0.772
Use of 2 or 3 stents for correction of LMCA lesion	11	8	0.085
Use of “kissing balloon” technique for final formation of bifurcation of the left main	16	17	0.175
Stenting of other coronary arteries	9	11	0.583
IABP	2	4	0.915

RESULTS

Angiographic success of the intervention was achieved in all patients. Clinical success was obtained in 96.6% of patients. Ventricular fibrillation developed in 1 patient from group II (implantation

of bare metal stents) 2 hours after the procedure. Nevertheless development of postresuscitation disease with multi-organ failure resulted in death of the patient from acute renal failure on day 8 after the intervention. Another group II patient had, along with severe stenosis of the left main (type 1,1,1) and also occlusion of the right coronary artery, and occlusion of terminal aorta leading to critical ischemia of lower extremities. He underwent aorto-bifemoral reconstruction with a bifurcation graft on the second day after stenting of the LMCA. Early postoperative period was complicated by continuous bleeding from distal anastomoses. Large amounts of blood products, including high dose of platelet concentrate, were administered without dose adjustment of antiplatelet drugs. Patient developed subacute thrombosis of the stent 3 days later and died. Only one access site complication was observed in a female patient from group II with development of extensive hematoma was successfully treated conservatively.

Long-term results are shown in the Table 5. Restenosis at the area of bifurcation of the left main developed in 2 patients (9.1%) in group I. One patient had restenosis in the LMCA after V-stenting, the second one – in the ostium of the CxA after "crush"-stenting. Both patients underwent successful balloon angioplasty.

10 patients (35.7%) from the group II developed restenosis: 8 of after "one-stent" stenting and 2 patients – after V-stenting. In 3 patients restenotic process involved the left main, the ostia of LAD and the CxA, in 2 patients restenosis was noted only in the LAD and in 5 patients – only in the CxA. Repeated endovascular revascularization was performed in 7 patients with restenosis (balloon angioplasty in 6 and implantation of drug-eluting stent in 1 patient). Three patients underwent coronary bypass surgery. In the follow-up period one patient from the second group suffered fatal AMI.

Table 5. Long-term results of interventions.

Unfavorable outcomes	Group I (n=22)	Group II (n=28)	Достоверность (p)
Restenosis	2 (9.1%)	10 (35.7%)	0.045
Repeated revascularization: PCI CABG	2 (9.1%) 2 (PTBC) 0	10 (35.7%) 7 (PTBC – 6. DES – 1) 3	0.045
AMI	0	0	
Mortality	0	1	1.000
Number t of patients with unfavorable outcomes	2 (9.1%)	11 (39.3%)	0.023

DISCUSSION

Atherosclerotic lesions located in the distal part of the left main are of special significance from two viewpoints. Firstly, it is the segment of the LMCA, i.e. the part of a coronary vessel which plays the most important role in myocardial blood supply. Secondly, this part includes bifurcation needing a special, "bifurcation" approach to be corrected. At the same time the bifurcation of the left main is not a trivial bifurcation. Usual approaches to the correction of "non-left main" bifurcation lesion implicates first of all the evaluation of the importance of all branches of bifurcation and the determination of the main and the side branches. While evaluating the importance of bifurcation branches, often it is impossible to determine which of them is main and which is side one. In the vast majority of cases, neither the LAD, nor the circumflex artery can be sacrified or and put under risk. Special significance of bifurcation in comparison with the ostium of the left main or the left main itself, is also determined by different long-term results after PCI. Thus, according to data of Sheiban I. et al. among the patients undergoing stenting of the left main with bare metal stents, restenosis developed only in those who had their lesions located at the bifurcation area (14). Therefore, the bifurcation of the left main is a special area and requires special approaches for interventional correction. It is not by chance that this bifurcation is sometimes called "the Great Bifurcation".

One of the most important problem to be solved before stenting is: whether it is possible to perform safe correction with implantation of one stent and subsequently consider the necessity of second stent implantation (so called "simple" correction) or it is necessary to immediately perform a "two-stents" ("complex") correction. We choose the second option, since the implantation of a second stent doesn't decrease the rate of MACE in the long-term, while increasing the duration of X-ray exposure, amount of contrast media administered, the risk of myocardial damage and also the cost of intervention (9,10,11).

Among the patients included in our study, the "simple" correction was performed in 39 cases. According to A.Medina classification most of them (22 patients) had 0.1.0 type of bifurcation lesion, less frequently (9 patients) 0.0.1 type was seen. "One-stent" correction was rarely used in other types of lesion (Table 6). Thereby, the "simple" stenting of the left main bifurcation was mostly performed in the cases when no significant stenosis was present in the ostium of one of the branches. there were two exceptions when this technique was used in true bifurcation lesions (type 1.1.1) made the exception. In both cases PCI was performed urgently in patients with ACS. One of the

Table 6. Correction of the left main bifurcation in different types of its lesion.

Type of correction	Type of bifurcation lesion						
	1.1.1	1.1.0	1.0.1	1.0.0	0.1.1	0.1.0	0.0.1
"One-stent"	2	2	1	1	2	22	9
V-, kissing-stenting	8	1	1	-	4	1	-
Crush-stenting	1	-	1	-	-	-	-
Y-stenting	1	-	-	-	-	-	1

patients previously underwent bypass grafting of an occluded marginal branch of the circumflex artery, second patient had poorly developed circumflex artery. PCI allowed for stabilization of patients' condition in both cases.

In two patients with lesions of types 0.1.0 and 0.0.1 initially chosen strategy had to be changed during the procedure: in one case the "one-stent" technqiue changed into V-stenting, in another case – into Y-stenting due to the dissection of the second branch and the left main developed during the intervention.

We have chosen "two-stents" correction in 17 patients since the risk of LAD or CxA closure while performing the "simple" stenting was extremely high. This was suggested for 10 patients with severe stenosis of distal segment of the left main extending to the ostia of the LAD and the CxA (type 1.1.1). Another 4 patients had severe stenosis of LAD and CA ostia and moderate stenosis (< 50% of the diameter) of distal part of the LMCA (type 0.1.1). Severe stenosis of the left main extended to one of its branches in 3 patients. Herewith the second branch was moderately stenotic (< 50% of the diameter). These patients were considered to have lesions of types 1.1.0 and 1.0.1.

When choosing the technique of "two-stents" correction we preferred V- (kissing-) stenting as this technique is simple and less risky. With its use the risk of side branch occlusion and hemodynamic instability is virtually absent. It is especially important in cases of urgent PCI in patients with ACS when even short-term (5-10 sec) disturbances of the blood flow in the LMCA may result in irreversible consequences (4). Such situation was seen in almost 30% of patients in our study. Using of "crush"-stenting technique minimizes the risk of side branch occlusion as well, but repeated introduction of the guidewire and balloon catheter into the side branch ostium covered with three layers of stents makes the procedure much more longer and complicated. These difficulties are the more expressed the less is the angle between the LMCA and the circumflex artery. Final formation of the left main bifurcation using "kissing balloon" technique in one of our patients failed just because of the above difficulties. Another disadvantage of "crush"-stenting is irregular coverage of bifurcation area with stents. At the side of the circumflex artery the left main is covered with three stent layers, while other segments of bifurcation are covered with one layer, hence, the use of drug-eluting stents leads to uneven drug and polymer concentration on the artery inner surface. The "culotte" technique is the most "elegant" and the most labor intensive and risky at the same time. First of all it makes certain requirements to stent design: stents with "closed cell" design and stents in which the lumen cannot be dilated up to the size of main branch of bifurcation (in cases of left main stenting the diameter of the main branch sometimes exceeds 4 mm) can't be used for performing of "culotte"-stenting (15). Technical difficulties and risk of this technique mainly consist in the fact that there is real threat of occlusion of one of the branches during alternate implantation of stents into the branches of bifurcation and repeated advancement of the guidewire through one or two layers of stents. As in the case with the "crush"-stenting, the "culotte"-stenting technique results in uneven coverage of the left main and its branches with stents: the left main coronary artery is covered with two layers of stents, while the branches – with one layer.

Taking into consideration first of all, the safety of our patients, as well as the above considerations concerning other techniques as well, when performing "two-stents" correction we used V (kissing-) stenting in most cases. Completely realizing that this technique also has several disadvantages (formation of metallic neo-carina) and limitations (extended left main stenosis), at the first stage of treatment of patients with lesion of the LMCA we have chosen this technique as the less risky one. We performed "crush" or Y-stenting only once when patients had long lesions of the LMCA extending for more than 5 mm proximally to the carina.

Follow-up examinations of patients from groups I and II revealed no significant differences between the groups in terms of long-term mortality rate. At the same time the use of DES for the correction of the LMCA bifurcation was connected with significantly lower rate of restenoses and the need in repeated revascularization. The obtained difference in the occurrence of restenoses and need in repeated revascularization (9.1% vs. 35.7%) were more significant than the similar difference seen in studies investigating the results of stenting for all segments of the left main (14, 17). Thus, it can be suggested that the use of DES for the correction of the left main bifurcation is more effective than for the correction of other segments of this artery. Confirmation of this suggestion undoubtedly requires larger and more detailed studies.

CONCLUSION

Endovascular interventions in lesion of LMCA bifurcation are associated with good angiographic and clinical results. The use of drug-eluting stents resulted in significantly lower rate of restenoses and need in repeated revascularization in long-term follow-up period after "simple" and "complex" correction of bifurcation of the left main coronary artery.

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Endovascular Myocardial Revascularization in Patients with Bifurcation Lesions of Coronary Arteries

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Our study included 135 patients with true bifurcation lesions of the coronary arteries. We compared immediate and long-term results of two treatment strategies: side branch provisional stenting and complex bifurcation stenting. Possible risk factors for corss-over from the provisional T-stenting technique to the complex bifurcation stenting technique were revealed and should be taken into account when planning endovascular revascularization of bifurcation lesions.

One of the complex problems of endovascular treatment for coronary heart disease is the reconstruction of the bifurcation lesions which account for about 15-22% of all types of the coronary lesions according to various data (1, 2, 3, 4).

During the last two years the rate of PCIs of bifurcation lesions in the various American and European clinics increased by 8% at the average (5).

Also it should be noted that the percentage of bifurcation stenoses in patients with multivessel coronary lesion is increasing every year (2,3).

Currently, due to improved equipment and the development of special techniques for bifurcation stenting, the indications for surgical intervention in CHD patients with complex coronary lesions hardly amenable for correction were reviewed in favour of endovascular interventions with entirely proved efficacy and safety (1-9).

The development of drug-eluting stents revolutionized percuteneous endovascular treatment of coronary lesions reducing the rate of repeated PCI after previous stenting procedures to 1-3% (10, 11). Antiproliferative drug-eluting stents contributed to the decrease of the main artery restenosis rate to 3-5% in patients with bifurcation coronary lesions. However the rate of side branch restenosis in the long-term follow-up period could not be reduced below 20% (1, 2, 3, 5, 9, 12, 13, 14, 16, 17).

Considering the above mentioned problems we would like to present the results of our study designed to investigate the efficacy and safety of different techniques of bifurcation stenting in CHD patients with true bifurcation coronary lesions.

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MATERIAL AND METHODS

Consecutive patients included in this study were identified from the didicated database where data were entered prospectivel since 2007 at the Department of Hospital Surgery of Peoples' Friendship University of Russia (head of the department professor Yu.V. Tarichko) at the N.A. Semashko Central Clinical Hospital No. 2, JSC «Russian Railways» (department of endovascular diagnostics and treatment methods, head of the department Z.H. Shugushev).

The study was planned to be performed in two stages. In general, the study involved 135 patients. During the 1st stage of study all patients underwent provisional T-stenting technique for correction of bifurcation lesions (n=68). Then we studied and analyzed clinical and angiographic results of performed procedures in order to determine risk factors of cross-over from the provisional T-stenting to complex bifurcation stenting. Based on this data analysis, differentiated approach to the treatment of bifurcation lesions was applied at the 2nd stage (77 patients) making it possible to define optimal strategy of the endovascular intervention.

The complexity of coronary lesions was evaluated using SYNTAX score. According to this evaluation, most patients (66%) were in moderate risk group (SYNTAX score 23-32).

Revascularization technique was discussed for each patient individually by a board of physicians including a cardiologist, a cardiac surgeon and an interventionist

The equipment used for the stenting procedure included 23 cm long and 8F diameter introducer, two coronary guidewiress advanced into the distal segments of the main and side arteries of bifurcation. All procedures were completed with final dilatation using “kissing balloon” technique.

Inclusion criteria: “true” bifurcation stenosis confirmed by quantitative angiography; de-novo lesions; side branch diameter more than 2.0 mm; stable effort angina of III-IV functional class according to Canadian classification; positive stress-tests; adequate drug therapy of CHD (intake of double antiplatelet therapy with cardiomagnyl 75 mg/day + clopidogrel 75 mg/day) at least 7 days before PCI.

Exclusion criteria: acute myocardial infarction; "false" bifurcation lesion; effort angina of I-II functional class; diameter of side branch less than 2.0 mm; severe heart failure; LVEF <40%.

Before PCI II patients underwent: 24-hour ECG monitoring, stress-tests (bicycle ergometry, transesophageal electrocardiostimulation), transthoracic or transesophageal EchoCG, EGD, selection of optimal drug therapy, coronary angiography. Myocardial viability in the territory of the infarct-related artery was evaluated in all patients surviving after myocardial infarction.

Laboratory control of cardiospecific enzymes (cardiac troponins T and I, CPK-MB) was performed on day 1 after PCI, and then control stress-testing and transthoracic EchoCG were carried out at in-hospital stage.

All patients were recommended to double antiplatelet therapy (clopidogrel 75 mg/day + cardiomagnyl 75 mg/day) after the discharge in addition to drug therapy for CHD for a period of at least 12 months.

Immediate results were evaluated according to the following criteria: absence of clinical presentations of III-IV functional class angina; negative stress-tests; absence of MACE (death, myocardial infarction, repeated target lesion revascularization – TLR, target vessel revascularization – TVR, coronary artery bypass grafting – CABG, negative cardiospecific enzymes on the first day after the procedure (troponin T and I, CPK-MB).

Long-term results were evaluated according to the following criteria: absence of angiographic in-stent restenosis as well as of clinical manifestation of III-IV functional class angina in at least 12 months after PCI; negative stress-tests; increase of exercise tolerance; absence of major adverse cardiac events (MACE).

The 1st stage of the study involved 68 patients, and the 2nd stage - 77 patients. In total 135 patients were included. Most patients were males – 91,4%. The mean age of all patients was 54.79±8.72 years.

In most cases (60%) bifurcation lesions of the left anterior descending artery (LAD) were found.

At the 2nd stage of the study the patients were divided into 2 groups. Group I involved 40 patients who underwent provisional T-stenting, and group II included 37 patients who underwent «complex» bifurcation stenting. The following techniques were used: T-stenting (n=25), V-stenting (n=5), "crush" (n=2), "mini crush" (n=2), "DKCRUSH" (n=3). 6 patients (8.6%) underwent bifurcation stenting of the left main and LAD using T-stenting technique in 5 cases and "crush" technique in 1 case.

Clinical characteristics of all patients are shown in Table 1.

Drug-eluting stents were implanted in all patientd at the site of bifurcation lesions (n=229), the most often used stents were Cypher ("Cordis", Johnson & Johnson) – 139, as well as Taxus ("Boston Scientific") – 70 and Promus stents ("Abott Vascular") – 10.

Angiographic characteristics of patients at the 1st and 2nd stages of the study are shown in Tables 2 and 3, respectively.

Results were statistically analyzed using MS Statistica 7.0. Student's t-tests, chi-square tests,

Table 1. Clinical characteristics of patients.

	Number	%
Effort angina of III IV FC	113 22	83.7 16.3
History of myocardial infarction	93	73.2
Heart failure (NYHA class)	70	55.1
Diabetes mellitus	17	13.4
Arterial hypertension	109	85.8
Smoking	103	76.3
Hypercholesterolemia	82	64.5
History of cerebrovascular accident	10	7.8

Table 2. Angiographic characteristics of patients (1st stage of the study).

Angle of bifurcation > 70° (of patients) < 70° (of patients)	 19 81
Calcification of the main artery (% of patients)	8.6
Calcification of the side branch ((% of patients)	17.5
The mean length of main artery lesion, mm	19.58± 3.41
The mean length of side branch lesion, mm	10.31± 4.89
Mean diameter of the main artery, mm	2.92± 0.29
Mean diameter of the side branch, mm	2.27± 0.19
The main artery lumen diameter narrowing, %	81.62± 7.36
The side branch lumen diameter narrowing, %	88.16± 9.16
Mean diameter of the main artery stent, mm	2.93± 0.83
Mean diameter of the side artery stent, mm	2.25± 0.00
Mean length of the main artery stent, mm	21.48± 3.55
Mean length of the side artery stent, mm	18.5± 0.7

Table 3. Angiographic characteristics of patients (2nd stage of the study).

	Group I n = 40	Group II n = 37
Angle of bifurcation > 70° (of patients) < 70° (of patients)	 0 6	 100 94
Calcification of the main artery, %	0	17
Calcification of the side branch, %	0	44
The mean length of main artery lesion, mm	18.78± 2.63	19.43± 2.99
The mean length of side branch lesion, mm	16.98± 2.86	25.54± 0.67
Mean diameter of the main artery, mm	3.00± 0.28	3.15± 0.42
Mean diameter of the side branch, mm	2.23± 0.11	2.6± 0.12
The main artery lumen diameter narrowing, %	80±6.12	81.22± 6.72
The side branch lumen diameter narrowing, %	82.3± 8.42	88.19±6.18
Mean diameter of the main artery stent, mm	3.00± 0.29	3.19±0.46
Mean diameter of the side artery stent, mm	-	2.75± 0.03
Mean length of the main artery stent, mm	20.88± 2.90	20.11±2.96
Mean length of the side artery stent, mm	-	23± 0.001
Mean pressure of balloon catheter inflation, atm	17.87± 1.4	18.72±1.09

Wilcoxon tests, Gehan tests, Kaplan-Meier tests, correlation analysis, log-linear analysis were used during processing.

RESULTS

During the 1st stage stenting procedure was successfully performed in 61 patients (89.7%). Complete myocardial revascularization was achieved in 88.2% of patients. There were no adverse cardiovascular events (MACE) observed during and after the procedure. Follow-up patient survival was 100%.

In 7 patients (10.3%) the procedure of provisional T-stenting finalized by the cross-over to complex bifurcation stenting which was performed using T-stenting technique in all patients. The most common reasons for the cross-over to complex stenting were: D-F type dissections, blood flow < TIMI 3, angina pain (including after final "kissing" dilatation), ECG signs of ischemia.

Significant increase of the main artery reference diameter was noted both after provisional T-stenting and after complex bifurcation stenting compared with similar parameters before PCI. Nevertheless, the diameters of the side branch were not different between both groups. However, comparison of these parameters in both group didn't reveal any significant difference ($p<0.05$) (Table 4).

Analysis of the results of provisional T-stenting at the 1st stage revealed risk factors contributing to the cross-over to complex bifurcation stenting (Figure 1).

As shown in the figure 1, the most significant factors are bifurcation angle <70˚, length of the side branch lesion >2.1 mm, diabetes mellitus, SYNTAX score and calcification of the side branch.

Table 4. Comparative analysis of reference diameters of main and side arteries.

	Pre-procedure	Post-procedure	P	До операции	После	P
	Provisional T-stenting			«complex» stenting		
Main artery diameter, mm	2.92± 0.29	3.15± 0.32	0.0042	2.94±0.16	3.18±0.28	0.003
Side branch diameter, mm	2.27± 0.19	2.53 ± 0.19	0.0823	2.48±0.21	2.62±0.23	0.0732

P>0.05

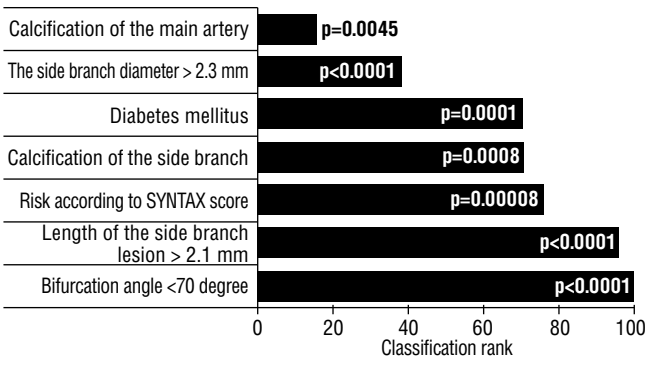

Figure 1. Distribution of risk factors by value.

Two patients from the group of complex bifurcation stenting had increased troponin T level on the day 1 after PCI without any ECG abnormalities. Mean level of troponin T was 0.18±0.06 ng/mL (diagnostic marker of MI was considered to be 3-fold increase of troponin T level).

Angina regression by less than two functional classes in post-procedural period at in-hospital stage was observed in 100% of patients (p=0.003).

Survival rate at the 2nd stage was 100% in both groups. Angiographic success was achieved in 97% of patients from group I and in 95% patients from group II. In spite of satisfactory angiographic results 1 patient from group 1 underwent implantation of the second stent in the side branch because of severe angina pain accompanied by ECG changes; after second stent implantation clinical signs of angina regressed. Intraoperative stent thrombosis was observed in 1 patient from group II after T-stenting of the circumflex artery and obtuse marginal branch.

In 3% of patients from group I and 11% of patients from group II an increase of the level of cardiospecific enzymes not accompanied by negative ECG changes was noted on first postoperative day (p=0.0032). Mean level of troponins was 0.2±0.003 ng/mL.

Comparative analysis of the results of stenting in both groups is shown in Figure 2.

As shown in the figure 2, complex stenting strategy was related to significant increase of cardiospecific enzymes level. However other parameters did not significantly differ between the groups.

Differences between these two groups in the postoperative period during the 2nd stage of study concerned only mean reference diameter of side branch, which was significantly larger after complex bifurcation stenting compared with provisional T-stenting, and was 3.24±0.11 and 2.61±0.16, respectively. Herewith left ventricle ejection fraction (LVEF) was not significantly different at any stage of the study compared with baseline data and its average values were 54.13±5.34 and 53.92±5.5%, respectively (p=0.6116).

Long-term results were evaluated in 70 patients – 62 males (88.6%) and 8 females (11.4%).

Patients were invited for repeated hospitalization for evaluation of long-term results. 9 patients were hospitalized ahead of schedule due to recurrence of clinical picture of angina. Observation period ranged from 12 to 18 months (mean observation period was 13.82±2.11 months) for all patients.

Thirty six patients (51%) received provisional T-stenting tretament and 34 patients (49%) underwent complex bifurcation stenting using T-stenting (n=22), V-stenting (n=5), "crush" (n=2), "mini-crush" (n=2), "DKCRUSH" techniques.

Overall survival was 100% in both groups. Follow=up exercise tolerance as well as left ventricle ejection fraction (LVEF) significantly increased in comparison with in-hospital period. According to the data of stress EchoCG with dobutamine, stenting of bifurcation coronary lesions contributed to the

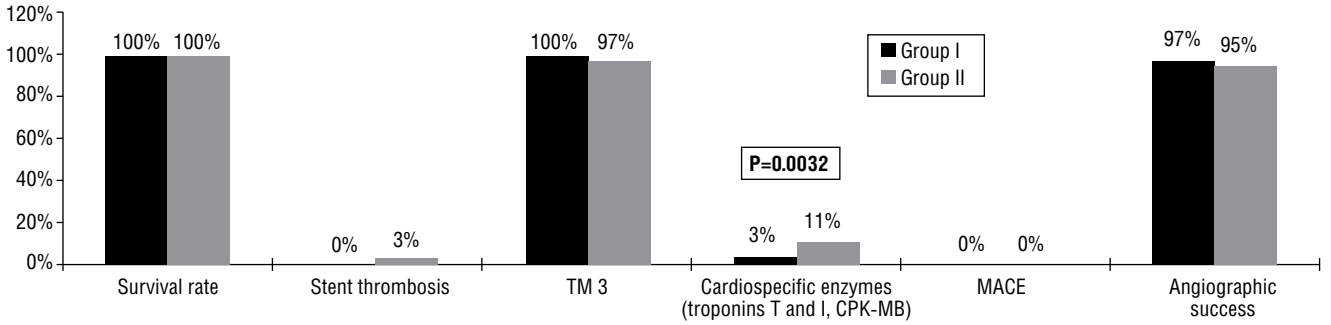

Figure 2. Comparative analysis of the stenting results at stage II.

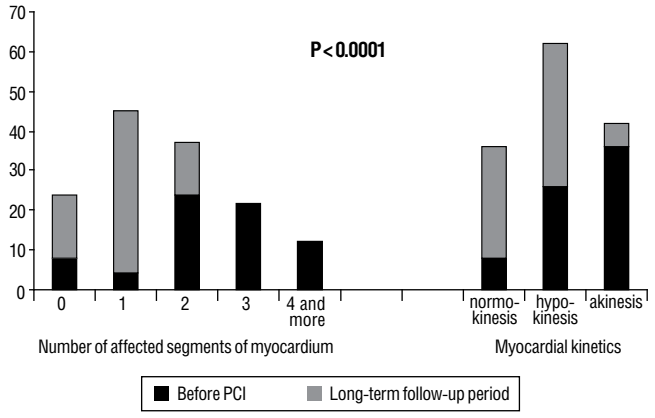

Figure 3. Development of myocardial kinetics.

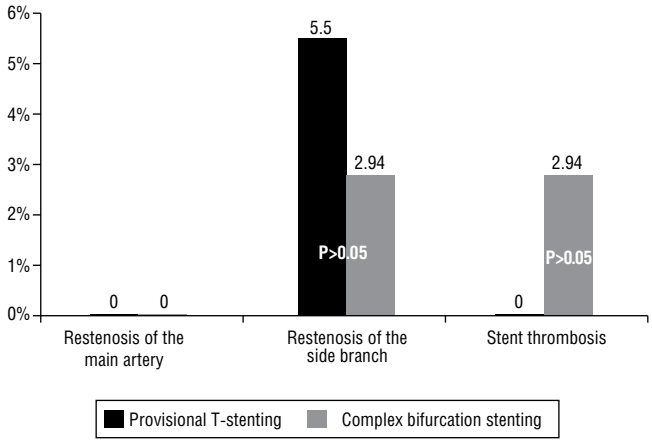

Figure 4. The incidence of stent restenosis and late thrombosis.

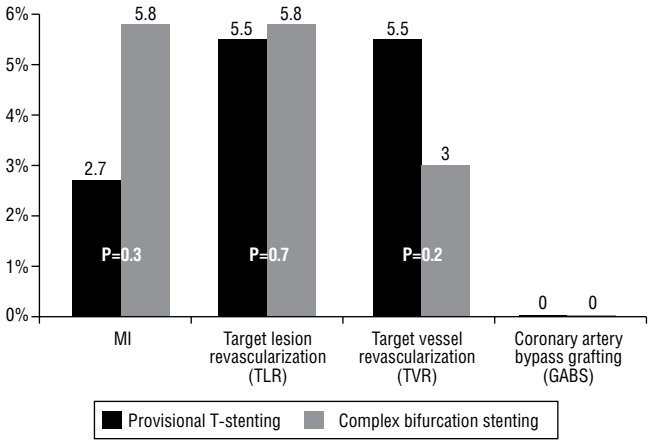

Figure 5. The incidence of repeated revascularizations and MI in the long-term follow-up.

improvement of myocardial kinetics and reduction of affected segments number in comparison with the pre-operative period (Figure 3).

Recurrent angina in the follow-up period was observed in 6 patients (16.6%) from the group of provisional T-stenting and in 3 patients (8.8%) from the group of complex bifurcation stenting, including patients with multivessel lesions and diabetes mellitus as well as 1 patient surviving after intraoperative stent thrombosis and 1 patient with blood flow TIMI 2 at the end of the procedure.

According to coronary angiography data, reasons for recurrent angina were: in 3 patients (4.3%) - in-stent restenosis at the bifurcation site, in 5 patients – progression of atherosclerotic process in other coronary arteries and in 1 patient (2,94%) – late stent thrombosis (Figure 4).

Repeated revascularization was performed in 7 patients. Herewith the target lesion revascularization (TLR) was performed in 5.5% of cases in the group of provisional T-stenting, and in 5.8% of cases in the group of complex bifurcation stenting. The target vessel revascularization (TVR) was performed in 5.5 and 3% of cases, respectively. It was decided not to perform repeated revascularization in two patients because of angina of I-II functional class.

In the follow-up period MI was observed in 1 patient (2.7%) from the group of provisional T-stenting and in 2 patients (5.8%) from group of complex bifurcation stenting. In 1 patient from the group of complex bifurcation stenting MI was caused by the thrombosis of “Taxus” stent developed shortly after discontinuation of clopidogrel (after 12 months) and in 2 other cases MI localization corresponded to the territory supplied by other coronary arteries (Figure 5).

As shown in the figure 5, there is a tendency for the increase of MI incidence in the long-term for the patients from the group of complex bifurcation stenting whereas the patients from the group of provisional T-stenting have a similar trend toward repeated target vessel revascularizations (TVR). However, comparison of these parameters in both groups didn’t reveal significant differences

MACE- (MI, repeated revascularization) and angina-free survival was 83.33% in the group of provisional T-stenting and 91.18% in the group of complex bifurcation stenting (p=0.3).

DISCUSSION

Implementation of stents with antiproliferative drug coating in clinical practice markedly improved the results of stenting of bifurcation lesions. The publication of promising results of bifurcation lesions stenting led to serious debates concerning optimal strategy for coronary intervention.

Currently the problem of side branch stenting expediency remains unsolved. Data from several clinical studies demonstrated that routine stenting of both bifurcation branches doesn't provide proper benefit in comparison with the strategy of side branch conditional stenting (2,3,5,7).

Evaluation of side branch should take into consideration the amount of myocardium supplied by this artery (2). In cases when the side branch supplies a large amount of myocardium, and residual ostial stenosis after the main vessel stenting reduces clinical efficacy of the procedure and ultimately leads to myocardial damage within this territory, restoration of blood flow in this artery should be considered (2,17). However when the occlusion of side branch doesn't lead to subsequent complications, further attempts to reopen the artery should be avoided (2,17,18,19).

There is increasing evidence that clinical and angiographic results are equal in either provisional T-stenting technique and complex bifurcation stenting technique (2-5,9,12-17). Also, the provisional T-stenting technique is noted to entail a low number of major adverse cardiac events (MACE) in the long-term, whereas, according to different authors, the use of drug-eluting stents allowed for the reduction of main artery restenosis rate to 2.9-3.5%. However the incidence of side branch restenosis remains high and ranges from 23 to 31.8% (1, 4, 5, 6, 9-12, 14, 17).

The note for cuation is distribution of plaque mass around the side branch ostium which may cause side branch occlusion during balloon catheter inflation due to "snow-plough" effect, which necessitates multiple balloon inflations including under high pressure (17, 18, 19). It often leads to exyensive dissection of the main artery intima and subsequent thrombosis (19).

Another unfavorable anatomic factor of bifurcation stenosis is lesion eccentricity. Irregular force distribution during balloon inflation due to eccentric lesion results in overdistension of opposite side of the vessel wall, impeding formation of intima tears on the plaque, and leads to elastic recoil of the artery which is one of the main causes of high rate of residual stenosis after balloon angioplasty (5,15,18,19).

Reimers et al. (2000), based solely on their own experience, suggested avoiding of routine stenting of both branches when the diameter of side vessel is <3.0 mm, and, on the contrary, considered the strategy of complex bifurcation stenting to be reasonable if side branch is ⩾3.0 mm.

Chen et al. (2009) recommended to perform stenting of side branch with diameter ⩾2.5 mm only in cases when the predilatation was complicated by dissection or occlusion.

TULIPE study demonstrated that bifurcation angle was the only predictor of side branch occlusion, while ignoring other important factors such as small diameter of side branch and lesion of side branch ostium (15).

In our study thanks to the use of drug-eluting stents the incidence of main artery restenosis was 0% and side branch restenosis rate was 2.94 and 5.5% ($p>0.05$) in the groups of provisional T-stenting and complex bifurcation stenting, respectively. Discovered eventual risk factors for provisional T-stenting technique allowed for a differential approach to selection of endovascular revascularization technique in this category of patients and thereby provided low rate of complications. Thus, the incidence of late thrombosis was 2.94% for patients from the group of complex bifurcation stenting. Herewith the rate of repeated target lesion revascularizations (TLR) was below 5.8% and target vessel revascularization (TVR) was 5.5%. Comparative analysis of endpoints for two strategies didn't reveal significant benefits with the use of any technique of bifurcation stenting.

Thus, safety and efficacy of drug-eluting stents is completely proved for patients with bifurcation coronary lesions, and their use allows for a substantial improvement of long-term results of PCI. Routine stenting of both vessels doesn't provide proper benefit compared with the strategy of provisional T stenting suggesting the truth of the principle "the less metal is better".

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Our Experience with Interventional Treatment of Hypertrophic Subaortic Stenosis

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Abbreviations:

HC – Hypertrophic Cardiomyopathy
LVOT – Left Ventricular Outflow Tracts
IVS – Interventricular Septum
LAD – Left Anterior Descending Artery
LVEF – Left Ventricular Ejection Fraction
LVEDD – Left Ventricular End-Diastolic Dimension
LVESD – Left Ventricular End-Systolic Dimension
LVPW – Left Ventricle Posterior Wall
LA – Left Atrium
EchoCG – Echocardiography

HC rate in the general population is 0.2% or 1 case per 500 subjects. HC is among the most common congenital cardiovascular diseases. Apart from long-term stable course, hypertrophic cardiomyopathy may have such complications as sudden death, acute and chronic heart failure, life-threatening heart rhythm disturbances. Obstacle in the left ventricular outflow tracts (LVOT) due to hypertrophic interventricular septum (IVS) in LVOT is one of the important pathogenetic mechanisms in this pathology.

Conventional pharmacotherapy not always allows fro effective control of disease symptoms, improve ment of heart function and elimination of the risk of life-threatening complications. In such cases a possibility of using different, non-pharmacological treatment approaches has to be considered. Till the end of 20th century the only effective treatment method was surgery with its high efficacy and low lethality (2). However, severe trauma due to “open” surgery, relatively long rehabilitation period and high number of complications led to the search for more sparing methods for HC treatment including transluminal chemical (ethanol) ablation. This intervention results in hemodynamic changes decreasing interventricular septum thickness, improving left ventricular outflow and decreasing the degree of mitral regurgitation (2, 3).

Transluminal chemical ablation of the first septal branch of LAD (left anterior descending artery) in HC was firstly performed in Russia at Volgograd Clinical Cardiology Centre (VCCC) on October 14, 1998 (4-6). This paper presents our clinical experience with endovascular treatment of HC patients.

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MATERIAL AND METHODS

Transluminal chemical ablation of the first septal branch of LAD was performed in 9 patients with HC. Patients’ age ranged from 42 to 67 years; there were 7 females and 2 males. Before surgery, all patients complained of weakness, significantly decreased exercise tolerance (50-100 m walking), heart pain on exertion (climbing 1-2 flights of stairs) and at rest (5 patients), breathlessness on slight exertion (4 patients) and at rest (2 patients), sense of shortness of breath (4 patients).

According to NYHA classification, before surgery 6 patients were in functional class (FC) IV and 3 patients - in FC III. ECG examination revealed sinus rhythm in all patients, left anterior bundle branch block in 3 patients, left ventricular hypertrophy with overload in 9 patients, enlargement of the left atrium in 2 patients.

The main method for diagnostics and determination of indications for surgery was Doppler echocardiography (EchoCG) with measuring of heart chamber dimensions, interventricular septum (IVS) thickness, the condition of the heart valves, left ventricular ejection fraction, and systolic pressure gradient between the left ventricle and the aorta. EchoCG revealed signs characteristic for HC in all patients. Before endovascular treatment, EchoCG examination demonstrated mean LVEF 69±12%, LVEDD 4.06±1 cm, LVESD 2.4±0.7 cm, IVS thickness 2.2±0.4 cm, LVPW 1.2±0.16 cm, LA 5.0±0.5 cm, systolic pressure gradient 88.3±29.4 mm Hg. Six patients had systolic anterior motion of the mitral valve cusp.

Patients received conventional conservative therapy before surgery: B blockers, ACE inhibitors, antiarhythmic and antianginal drugs, diuretics, drugs improving metabolism. By the time of operation medical treatment was ineffective.

The indications for endovascular treatment were: ineffectiveness of conservative therapy; resting systolic pressure gradient above 50 mmHg; IVS thickness at LVOT more or equal to 1.8 cm; suitable anatomy for endovascular intervention.

All procedures were performed at cath lab (BICOR TOP, Siemens) under intravenous and local anesthesia.

The femoral artery puncture by Seldinger’s approach was performed in all cases. Heparin 75-100 IU/kg was administered to all patients after introducer placement for prevention of arterial thrombosis. In addition, transvenous introduction of electrode into the right ventricle was performed for temporary pacing in case of complete atrioventricular block.

Then all patients underwent selective left and right coronarography according to standard technique. The purpose of the coronary angiography was to evaluate coronary anatomy including the diameter and location of septal branch as well as of the lesions of coronary vessels, which were not observed in our patients. Selective coronary angiography of the left coronary artery in the views providing the best visualization of the septal branch supplying the hypertrophied part of IVS was performed throught the inserted guiding catheter (Figure 1). Septal branch catheterization was performed using 0.014-inch guidewire; dual-lumen balloon catheter was introduced over this guidewire inserted in the distal part of the septal branch with subsequent positioning in the proximal part of the septal branch (Figure 2). Under EchoCG guidance, contrast medium (Omnipaque, 2 3 mL) was injected through the central lumen of balloon catheter for more precise definition of the territory and amount of myocardium supplied by the septal branch. It should be noted that injection of conventional iodium-containing contrast agent into the septal branch often allows to define the supplied territory by means of EchoCG. Then balloon dilatation within the septal branch was performed and contrast agent was injected through the central lumen of catheter. Thus, the absence of reflux to the LAD was achieved (Figure 3). Non compliance with this condition may lead to burn of LAD intima with ethyl alcohol with enfollowing fatal complications. Patients received intravenous narcotic analgetics before the chemical ablation to reduce the pain syndrome.

Then we slowly (over 1-2 min.) injected 1-3 mL of absolute ethyl alcohol into the septal branch. The balloon remained dilated for at least 5 minutes after ethanol injection. After deflation of the balloon, control coronary angiography of the left coronary artery was performed and the procedure was finished if occlusion of the septal branch was achieved (Figure 4). Ethanol injection led to significant increase in myocardial density on EchoCG (Figure 5, 6). After completion of the procedure, patients were transferred to intensive care unit for at least 18 hours. If atrioventricular block was not observed during this time period and patient's condition was stable, the electrode for temporary pacing was removed and the patient was transferred to cardiology department.

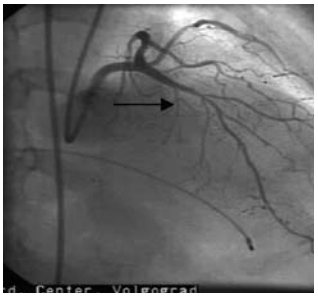

Figure 1. Selective coronarography of LCA. The arrow indicates 1 septal branch.

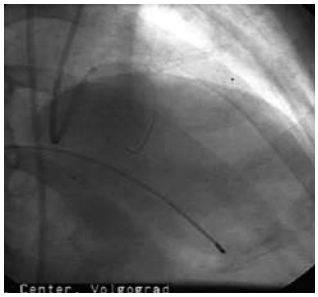

Figure 2. Catheterization of the septal branch with guide wire.

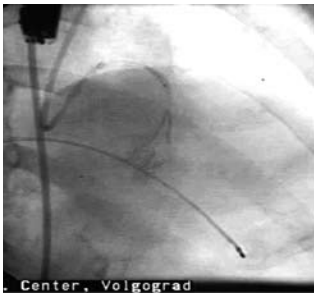

Figure 3. Balloon dilation within the septal branch during injection of the contrast medium.

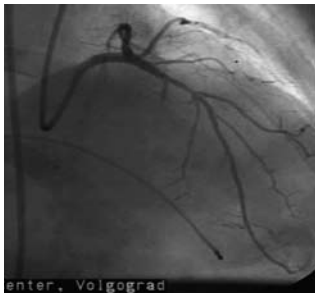

Figure 4. Occlusion of the septal branch after injection of ethyl alcohol and absence of reflux to LAD.

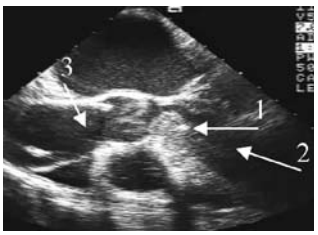

Figure 5. EchoCG before chemical ablation.

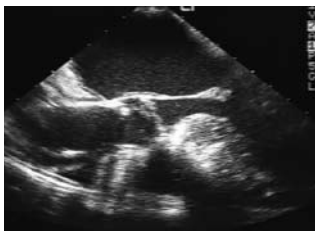

Figure 6. EchoCG after chemical ablation.

1. Hypertrophic part of IVS. Reduction of IVS size and enlargement of the left ventricle output part.
2. Left ventricle
3. Aorta

RESULTS

Successfu; transluminal chemical ablation of the first septal branch confirmed by control coronary angiography was performed in all patients.

ECG examination in early postoperative period revealed sinus rhythm in 7 patients, complete right bundle branch block in 4 patients, signs of myocardial ischemia in the upper lateral parts of the left ventricle in 6 patients

Two patients developed complete atrioventricular block after ablation. Implantation of permanent two-chambered pacemaker EKS 4000 was performed in one female patient. Temporary pacing in another critically ill female patient was complicated by repeated electrode migration from the right ventricle due to extremely hypertrophied myocardium and the impossibility to fix the electrode tip, which finally led to patient's death.

In early postoperative period EchoCG examination demonstrated mean LVEF 66.3±11.7%, LVEDD 4.18±1.04 cm, LVESD 2.5±0.7 cm, IVS thickness 1.97±0.27 cm, LVPW 1.18±0.27 cm, LA 4.8±0.41 cm, systolic pressure gradient 52.3±28.7 mm Hg. Five patients had systolic anterior motion of the mitral valve. Systolic pressure gradient was not decreased but, conversely, increased by 19% compared to baseline in 1 patient in one day after the procedure. Gradient decrease was observed in this patient from the 4th day only.

Patients reported improvement at discharge: 5 patients were in FC II and 3 patients in FC I according to NYHA classification.

In the long-term period (follow-up from 2 to 5

years) 8 patients were examined. Subjectively all patients reported significant improvement after performed procedure. Exercise tolerance increased; heart pain on exertion (climbing 3-4 flights of stairs) was observed in 2 patients. Insignificant dyspnea on exertion (walking 200 m) was observed in 3 patients. No major cardiac complications were reported during the follow-up period. Clinical and functional status of patients according to NYHA classification: FC I in 4 patients, FC II in 4 patients (before surgery 6 patients were in FC IV and 3 patients in FC III).

ECG examination revealed sinus rhythm in 7 patients, complete right bundle branch block in 3 patients, signs of myocardial scarring in the upper lateral parts of the left ventricle in 4 patients (I, AVL). One female patient had paced rhythm (using EKS 4000).

In the long-term period (follow-up from 2 to 5 years) EchoCG examination demonstrated mean LVEF 65.75±5.28%, LVEDD 4.47±0.38 cm, LVESD 2.5±0.5 cm, IVS thickness 1.8±0.21 cm, LVPW 1.1±0.29 cm, LA 4.7±0.43 cm, systolic pressure gradient 36.8±18 mm Hg.

Systolic anterior motion of the mitral valve cusp persisted in 3 patients. Certain EchoCG parameters of patients are shown in Table 1.

Thus, EchoCG examination before surgery and in the long-term follow-up after endovascular treatment revealed reduction of IVS thickness from 2.2±0.4 cm to 1.8±0.21 cm, decrease in systolic pressure gradient from 88.3±29.4 to 36.8±18 mm Hg. Systolic anterior motion of the mitral valve was observed in 6 patients before surgery and in 3 patients only in the long-term follow-up.

Table 1. EchoCG data for HC patients before surgery, in early postoperative period and in long-term follow-up.

Patient	Age	IVS at LVOT (cm)				LVOT gradient (mmHg)				Systolic anterior motion of the MV		
		before	p/o	p/o	2-5 years	before	p/o	p/o	2-5 years	before	p/o	2-5 years
1	61	2.9	2.4	Death		70	80	Death		-	Death	
2	42	2.5	2.3	2.3	1.7	65	25	25	23	+	+	+
3	51	1.9	1.6	1.6	1.5	80	16	16	16	+	+	-
4	46	1.8	1.7	1.7	1.7	65	35	35	30	+	+	+
5	47	2.1	2.0	2.0	2.0	88	71	71	62	+	+	+
6	42	2.1	2.0	2.1	2.1	160	50	50	35	-	-	-
7	67	1.8	2.1	2.0	2.0	77	90	90	48	+	+	-
8	54	2.5	1.7	1.7	1.6	100	81	81	60	+	-	-
9	61	2.2	2.0	2.0	1.9	90	23	23	20	-	-	-
mean	52.3 ±9	2.2± 0.4	1.97± 0.27	1.97± 0.27	1.8± 0.21	88.3± 29.4	52.3± 28.7	52.3± 28.7	36.8± 18			
		P<0.03		P>0.08		P<0.05		P>0.16				

DISCUSSION

Transluminal chemical ablation is an alternative method of treatment for refractory obstructive HC. According to literature data, the rate of successfully performed interventions is high and comparable to the results of surgical myectomy (7, 8). Transluminal chemical ablation has a number of advantages: no cardiopulmonary bypass is required, hence, there is no risk related to it, shorter in-hospital stay and rehabilitation period, reduced expenses. It may be performed in elderly subjects and patients with severe comorbidities.

Potential disadvantages include: the risk of the left coronary artery injury; the development of atrioventricular block requiring implantation of pacemaker in 10-20% of patients (9, 10, 11, 12); catheterization or identification of target septal branch is technically impossible in number of cases; low success rate in patients with great septal thickness and anomalies of the mitral valve cusp or papillary muscles (13, 14, 15, 16).

It should be noted that we used endovascular treatment of HC only in cases when conservative therapy options were exhausted and patients' condition progressively worsened. Such management allowed to avoid aggressive (interventional and surgical) methods of treatment in many patients, significantly improve both subjective and functional condition and disease prognosis.

Thus, only patients in whom conservative therapy was ineffective were referred for interventional treatment.

Assessing the results of TLCA in general, we can note that this intervention represents the method which is well tolerated by patients, provides significant clinical benefit and improves functional status of patients. However, the degree of such improvements depends considerably on accuracy of indications, diagnostics and precise intervention. Thus, our first observations were associated with complications in the form of complete atrioventricular block, and one death as a consequence. In the first case, we believe the cause of such complications to be related to our intention to obtain complete occlusion of the septal branch at the orifice and hence to larger volume of ethanol injected (3 ml), and in the second case to insufficient attention to possible postoperative arrhythmia and its management in the presence of extremely hypertrophic left ventricular myocardium.

Subsequent cases were not associated with such complications because the amount of ethanol injected was decreased to 1.5-2.0 ml and prevention of arrhythmia became effective. It should be noted that LV-Ao systolic pressure gradient in one patient tended to increase immediately after surgery rather than to decrease over time like in majority of cases. This patient was relatively young. We believe this phenomenon to be caused by more marked inflammatory response to intervention in relatively young patient and, hence, by relatively greater edema in LVOT. Later the gradient decreased with anti-inflammatory

therapy, and although this decrease was insignificant the other indices in this patient improved significantly and with marked positive clinical result.

Our experience demonstrated that radicalism should be avoided during TLCA performing, there is no necessity to obtain angiographically "pretty picture" if the effect is already achieved according to ECG and a sufficient maximum of ethanol is injected. Excessive aggressiveness is only detrimental for the efficacy and safety.

CONCLUSION

The incidence of complications of ablation decreases with experience gaining. Generally, the use of this method allows to obtain good clinical effect, to prevent severe complications and to improve the prognosis in significant number of extremely severe HC patients in whom conservative therapy was ineffective. Our results with transluminal chemical ablation (TLCA) of the septal branch of LAD in HC patients demonstrate the efficacy of this method in critically ill patients.

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Transcatheter Closure of Atrial Septal Defects Using Mesh Occluders: the Causes of Our Failures

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Abbreviations:
CHD – congenital heart defect
ASD – atrial septal defect
IAS – interatrial septum
RA – right atrium
ECG – electrocardiography
EchoCG – echocardiography

Relevance of the topic: according to various authors' data, the rate of atrial septal defect (ASD) amounts to 5-15% of all congenital heart defects (CHD) (3, 4, 5, 7, 8, 10, 14, 15). Before the 1990s the gold standard for ASD management was surgery accompanied with low lethality and small rate of complications (6, 8, 12, 13). However, surgical treatment is associated with major operative trauma, cosmetic problems (especially for women) and requires rehabilitation period. Transcatheter closure of secondary ASD was first successfully performed by King in 1974, but it has become widely used in the world in the last decade only (1, 8). Further development of transcatheter technique and development of new occluding devices currently made transcatheter closure of secondary ASD an alternative to surgical intervention (1, 2, 8, 9, 11, 16).

However, despite significant improvement of endovascular devices and methods that broaden the capabilities of interventional techniques, the rate of failed attempts during ASD management varies from 2% to 6% according to various authors (2, 8, 9). This study was dedicated to the analysis of causes of failures observed in our experience with endovascular treatment of ASD.

MATERIAL AND METHODS

Endovascular surgery in patients with ASD, using Amplatzer systems and recently HeartRTM occluders as well, has been performed in the Department of Endovascular Surgery and Angiography of the Volgograd Regional Clinical Cardiology Centre since October 2003 till now.

A total of 140 surgical procedures of ASD closure in patients aged from 7 months to 62 years (with mean age of 11.2±1.3 years) were conducted in the department: in 104 female subjects (74.3% of total number of patients) and 36 male subjects (25.7% of total number). The indications for endovascular treatment of patients were as follows: secondary ASD with well-defined edge of the defect, diameter of the defect not more than 40 mm.

Prior to surgery, besides general clinical examination, all patients underwent instrumental diagnostic methods including: ECG, chest X-ray, transthoracic and/or transesophageal echocardiography (EchoCG).

All interventions were performed under double control (EchoCG and fluoroscopy). Intraoperative EchoCG was mandatory for the selection of adequate device during ASD closure. EchoCG was crucial for positioning of occluder and checkup of procedure results during the endovascular intervention.

Transesophageal EchoCG was used at cathlab in 22 cases (amounting to 16.3% of total number of patients). Transthoracic EchoCG was used in 84.3% of cases (118 patients).

Endovascular ASD closure failed in seven (5.0%) of 140 patients who underwent intervention. These patients were from older age group in 5 cases: their mean age was 22±10.8 years (minimum age was 12 years and maximum age was 47 years); in two cases the patients were three years old.

According to transthoracic EchoCG, each of seven patients had central haemodynamically significant ASD. Mean diameter of the defect was 1.8±0.5 cm (with minimum of 0.9 cm and maximum of 2.6 cm). Mean size of the superior rim was 1.15±0.2 cm (with minimum of 0.8 cm and maximum of 1.5 cm), mean size of the inferior rim was 0.84±0.4 cm (ranging from 0.5 cm to 1.6 cm), mean size of the aortal rim was 0.26±0.03 cm (ranging from 0.2 mm to 0.4 cm), mean size of superior vena cava rim was 1.56±0.4 cm (minimum – 1.2 cm, maximum – 2.0 cm) and mean size of inferior vena cava rim was 1.7±0.6 cm (minimum – 0.9 cm, maximum – 2.3 cm). Thereby, the sizes determined by transthoracic EchoCG met criteria according to which indications for endovascular ASD closure using Amplatzer device were established.

Following preoperative examination, all patients underwent elective endovascular intervention performed according to standard technique. Amplatzer occluder was not used in one case (out of seven) in a 12- years-old girl, because measuring balloon waist could not be determined and transthoracic EchoCG revealed left-to-right shunt at the inferior rim edge of the defect. ASD measuring 4.0x 2.5 cm was found during open surgery, the defect rim near the inferior vena cava was absent, while according to preprocedural transthoracic EchoCG the diameter of ASD was 2.5 x 2.7 cm and the inferior rim near the inferior vena cava measured 0.9 cm.

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The attempts of occluder implantation in other patients failed due to different reasons. Three patients had the following problems:

1. Dysfunction of mitral valve due to the prolapse of left atrial disk of the device was observed in a 3-years-old girl after septal occluder deployment;
2. Complete deployment of occluder disks could not be achieved in a 12-years-old female patient and this caused serious rhythm disturbance on ECG;
3. After the implantation the occluder could not be optimally positioned in a 46- years-old woman, and test tractions led to occluder dislocation into the right atrium (RA). A complication in the form of hemopericardium was observed in the same patient after endovascular attempt. (During the open surgery for defect correction a through defect 0.5 mm in diameter was found near the left atrial appendage; it was sutured).

In all these three cases the occluder was removed and the patients underwent open surgical correction. During surgical revision of the interatrial septum a defect with absent inferior rim was visualized in all three patients. However, according to preoperative transthoracic EchoCG data, the defect was centrally located and possessed a good inferior edge.

In the fifth case (15-years-old female patient) the waist on the measuring balloon could not obtained (see Fig. 1a). Therefore, we had to measure the defect diameter by means of intraoperative transthoracic EchoCG, and the attempt of septal occluder implantation on the base of EchoCG data was unsuccessful (see Fig. 1b). During occluder implantation we failed to achieve optimal deployment of the disks and steady occluder's position within the defect. We suggest that it was related to inadequate size of IAS which prohibited optimal deployment of the left atrial disk, which, in its turn, led to the deformation of the entire device and made its implantation impossible.

In the sixth case (24-years-old female patient) displacement of the right atrium disk into the RA was observed during test tractions of implanted occluder, as a consequence the device was removed. ASD with soft distensible mobile edges was revealed during open surgery in both patients (15- and 24- years-old).

Let us review in details the seventh case. A 3-years-old boy was admitted to our clinic with the diagnosis: *CHD. ASD-II. Circulatory failure, grade I*. The patient underwent preoperative examination including transthoracic EchoCG. *RV 2.8 cm, RA 3.5 cm. Conclusion: Atrial septal aneurysm with a defect 0.8x1.2 cm in diameter. Inferior rim – 1.0 cm, superior rim – 1.0 cm, superior vena cava rim – 1.0 cm, inferior vena cava rim – 1.3 cm, aortic rim – 0.3 cm. Insignificant pulmonary arterial stenosis (SPG 40 mm Hg). Dilatation of the right heart*. The boy underwent elective intervention. ASD diameter was 13 mm when measured with catheter measuring balloon. (see Fig. 2a). HeartR™ occluder of 14 mm diameter was selected and implanted in the projection of the interatrial communication (see Fig. 2b). However,

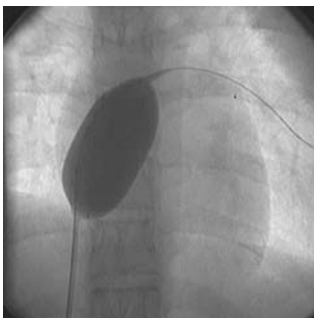

Figure 1a. The moment of balloon inflation within interatrial defect. During maximal balloon inflation the waist is not seen.

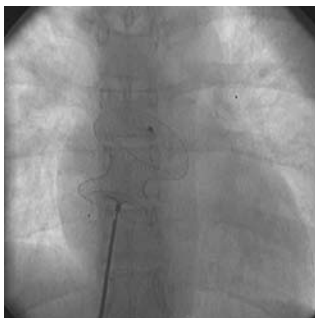

Figure 1b. The moment of attempt of Amplatzer occluder implantation (delivery system is not detached). The occluder disks are not totally deployed.

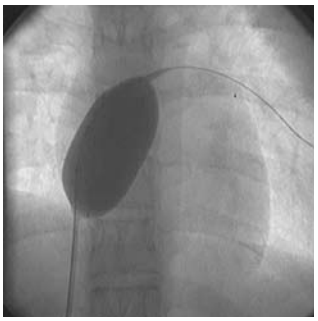

Figure 2a. The moment of balloon inflation within interatrial communication. The balloon waist is visible.

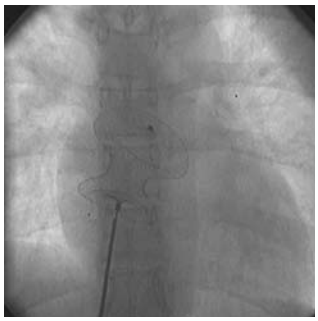

Figure 2b. Implanted HeartRTM occluder (the delivery system is detached).

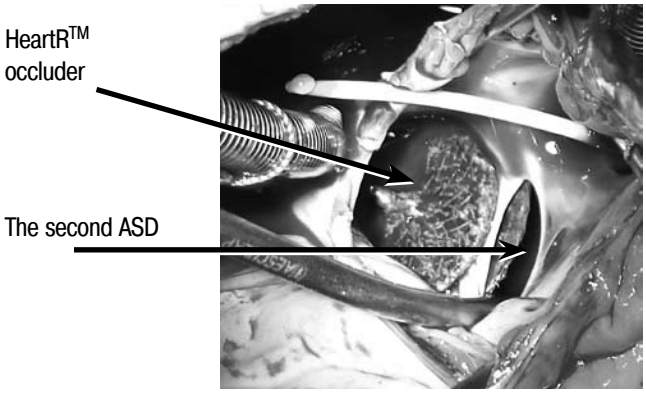

Figure 3. Two ASDs during open surgery. The first defect contains HeartR™ occluder.

the delivering system detachment led to a small displacement of the upper part of the occluder into the RA cavity, and there were signs of minimal shunt above the upper edge of the occluder (revealed by control transthoracic EchoCG).

Observation over time showed occluder displacement towards the RA and a significant left-to-right shunt which necessitated surgical intervention under cardiopulmonary bypass because we suspected occluder dislocation. During the operation two ASDs were revealed. The septal occluder was placed within one of them without signs of dislocation, while the second defect was separated from the first one by a bridge, located in the area of its superior edge, and was slit-shaped (dimensions 1.0x0.3 cm) (see Fig. 3).

The boy underwent the repair of IAS with autopericardial patch.

DISCUSSION

The analysis of causes of our failures in endovascular ASD repair demonstrated that they could be divided into 2 mutually dependent elements.

1. Insufficient preoperative assessment of defect anatomy. Among 7 failed attempts the rims of the defect were incorrectly assessed in 4 patients and the second septal defect was not revealed in the fifth case. Three patients were adults, and assessment of defect anatomy was transthoracic. In all of 5 patients this led to incorrect evaluation of inferior rim and the anatomy of the defect, which was the cause of failure. We concluded that transthoracic EchoCG can provide inaccurate data even with apparently good visualization of intracardiac structures. Currently we use transesophageal EchoCG in all adult patients. This allowed to refuse endovascular intervention for a number of patients at preoperative stage preoperatively, in spite of the data of transthoracic EchoCG which favored indications to interventional treatment.

2. In our opinion, the structure and mechanical "rigidity" of IAS into which the occluder will be implanted, constitute an important issue of preoperative assessment. We faced two cases when preoperative EchoCG demonstrated an ASD with sufficient rims, but while measuring the defect size with balloon catheter the diameter could not be assessed because of absence of balloon waist at maximum inflation. In one of these cases we nevertheless tried to implant occluder on the base of EchoCG data and intentionally used an occluder larger than the EchoCG defect diameter. However during test tractions the occluder migrated into the RA and could not be firmly fixed within the IAS. Both patients underwent open surgery during which IAS with very elastic thin "cigarette-paper" edges was revealed, and inferior rim of the defects was poorly developed.

We suppose that occluder implantation on the base of EchoCG data only, when it is impossible to measure the defect with balloon catheter, should be considered with utmost caution and on the individual basis, taking into consideration anatomical features and possible complications for each case.

Another important recipe for the success of transcatheter ASD closure is the availability of occluders of all sizes in the operating room because preoperative data may sometimes significantly differ from intraoperative data.

CONCLUSIONS

- Transesophageal EchoCG must be an obligatory stage of preoperative examination of adult patients in whom the use of endovascular occluders is considered;
- In case of mobile distensible ASD rims, when it is impossible to determine the defect size with measuring balloon catheter, implantation of occluder should be refused or it should be performed very carefully after more precise definition of all defect details according to EchoCG;
- Endovascular ASD closure is a modern minimally traumatic and effective method for this defect correction, allowing to achieve good result in 95% of patients.

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Efficacy of the Treatment of Pulmonary Embolism Depending on the Time of Patients' Admission

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The efficacy of the treatment of pulmonary embolism was compared in 138 patients in relation to the intensity of pulmonary embolic lesion, presence of risk factors and time of the thrombolytic therapy initiation. Data analysis revealed values of pulmonary pressure to be maximal in patients with later admission to the hospital and thrombolytic therapy (TT) initiation. Similar dependence was shown for the regression of clinical evidence of pulmonary embolism. In patients who had appealed for medical aid within a month, pressure in the pulmonary circulation (PC) decreased to normal values (25-29 mmHg), whereas in patients with late admission and TT initiation (from one month up to one year) the pressure remained high and main clinical signs of pulmonary embolism did not regress.

Pulmonary embolism (PE) is one of the most important clinical problems. It is one of the most disastrous complications which suddenly kills many patients.

At present practical significance of PE problem is determined firstly by evident increase of pulmonary embolism occurrence in various diseases and secondly by the fact that PE is becoming the third most common cause of death in industrial countries, after myocardial infarction and stroke, and has 30% death-rate in case of absence of timely medical care (4, 9).

Clinical relevance of PE problem is determined not only by the severity of this disease and high mortality rate, but also by the difficulties in timely diagnostics of this complication due to polymorphism of developing clinical syndromes. According to data of numerous pathologic examinations in 50-80% PE is not diagnosed at all and in many cases only a presumptive diagnosis of PE is made (1, 2, 5).

The survival criterion is currently used for the assessment of efficacy of massive PE treatment. According to S. Rich (11,12) pulmonary embolism doesn't cause any serious consequences and chronic pulmonary hypertension develops in no more than 1% of cases. However according to data of V.S. Saveliev et al. (7), despite of timely performed conservative treatment chronic occlusion (stenosis) of the pulmonary trunk or its main branches occurs in 70% of cases with the development of severe hypertension in pulmonary circulation. Multicenter study ICOPER (10) showed the possibility of poor outcome to be high also in the long-term period after an acute PE episode. Mortality in 3 months after the treatment was 7.9%. The primary cause of death in the follow-up period after acute PE was right ventricular failure due to the development of chronic postembolic pulmonary hypertension and formation of chronic cor pulmonale. Total recovery is observed only in the cases when patency of arterial pulmonary circulation is restored by thrombolytic and anticoagulant therapy, or even spontaneously, resulting in normalization of hemodynamics (7, 9, 13). Some authors (6,8) suggest the triggering aspect of chronic postembolic pulmonary hypertension (CPEPH) development to be large thrombotic embolus with organization signs entering the vessels of PC. Due to its morphologic features this embolus doesn't undergo fragmentation in the right ventricle and enters the pulmonary trunk in one piece; then it becomes fixed in the pulmonary arterial branches, as a rule – at bifurcations, resulting in severe luminal narrowing of the vessel or its complete occlusion. Over time thrombotic embolus strongly accretes to vessel wall and is covered with the layer of neointima. Its structural change continues for many months and results in the formation of connective tissue cords, plaques and membranes in the pulmonary vessels representing an obstacle of different degree for the blood flow.

The following clinical and historical data are considered to be predictors of CPEPH development: recurrent course of pulmonary thromboembolism, long-standing venous lesion (thrombophlebitis or phlebothrombosis), severity of acute PE, overweight, and (in women) – the intake of oral contraceptives and clinical presentations of thrombotic embolism at early puerperal period (3).

Analysis of clinical outcomes in patients, who has suffered PE, is of great practical significance for health care service allowing for the determination of optimal approach to the treatment and prevention of PE.

Our study was aimed at comparative evaluation of postembolic pulmonary hypertension occurrence depending on the severity of pulmonary embolic

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lesion, the risk factors and the time of thrombolytic therapy initiation as well as the degree of clinical symptoms regression in our patients.

MATERIAL AND METHODS

Five hundred and thirty five patients diagnosed with pulmonary embolism confirmed by pulmonary angiography (PA) were treated in Krasnoyarsk Regional Clinical Hospital in the period of time from 1992 till 2009. 138 patients (76 females and 62 males) were selected by blind sampling procedure for detailed analysis of treatment efficacy. Patients' age ranged from 19 to 77 years (with mean of 48±19 years).

Time of admission and time period from the onset of clinical manifestation of pulmonary embolism to the initiation of thrombolytic therapy were determined for all patients, the degree of pulmonary hypertension was correlated with the duration of this period, concomitant risk factors, and changes in clinical presentation during the treatment.

The first study group consisted of 102 patients admitted to the hospital at early stages of the disease (<1 month from the onset of symptoms); these were 74% of all patients included in the study. More than a half (71, that is 69.6%) of 102 patients were hospitalized within one week after the onset of clinical symptoms. 31 patients (30.4%) from other city and regional clinics were hospitalized within one month after the onset of symptoms development.

The second group consisted of 36 patients admitted at later stages, from 3 months to one year.

The examination of medical history allowed for the determination of the following risk factors (Table 1).

All patients underwent urgent pulmonary angiography with simultaneous invasive blood pressure measurement. Taking into consideration the fact that embologenous thrombus is mostly located at iliocaval segments or at proximal portions of the veins of lower extremities, implantation of cava filter in infrarenal position of the inferior vena cava was performed for prevention of thromboembolic events recurrence. Massive one- or two-sided PE with pulmonary hypertension of different degree was revealed in patients during PA (fig. 1). Patients with catheter inserted into the trunk of pulmonary artery were admitted to Cardiac Intensive Care Unit for selective thrombolysis at a dose of 3000000 IU (unless contraindicated) with subsequent control of direct pressure in the trunk of pulmonary artery (Table 2).

In order to determine the factors influencing the efficacy of thrombolytic therapy we compared time of admission to the hospital and risk factors revealed in patients (Table 3).

RESULTS AND DISCUSSION

After the analysis of clinical presentation, risk factors (phlebothrombosis, trauma, operative interventions, malignancies, chronic heart failure, COPD and recurrent PE) and time of admission and their

Table 1. Risk factors in patients with PE.

Risk Factors	Group I, n=102		Group II, n=36	
	abs.	%	abs.	%
Phlebothrombosis	87	85.3	32	88.8
CHF	21	20.6	21	58.3
COPD	30	29.6	23	63.8
Obesity	15	14.7	8	22.2
Tumors	3	2.9	1	2.7
Trauma	2	1.9	6	16.6
Surgery	4	3.9	2	5.5
Oral contraceptives intake	6	5.8	-	-
Recurrent PE	4	3.9	28	77.8

Table 2. Change in hemodynamic parameters of pulmonary circulation after TT.

Time of admission	SPPA before TT, mmHg			SPPA after TT, mmHg		
	max syst.	min syst.	mean	max syst.	min syst.	mean
Day 1	98	25	56±22.1	35	22	27±4.8
Day 3	95	21	51±18.8	38	22	29±5.5
Day 7	105	25	57±19.9	45	24	30±6.2
Day 14	87	52	69±19.1	58	22	38±14.7
1 month	90	32	55±18.7	60	21	36±12.9
3 months	93	24	65±22.9	58	25	44±11.7
6 months	109	75	83±11.9	82	39	50±21.1
1 year	111	95	103±11.3	97	76	86±14.8

Figure 1.

Table 3. Distribution of risk factors in patients of two groups.

Risk factors	Group I, n-102			Group II, n-36		
	1st week	2st week	1 month	2 months	3 months	1 year
Phlebothrombosis <3 months	57 (55.9%)	6 (5.8%)	5 (4.9%)	-	-	-
Phlebothrombosis >3 months	3 (2.9%)	5 (4.9%)	11 (10.7%)	29 (80.5%)	6 (16.6%)	1 (2.7%)
CHF	5 (4.9%)	4 (3.9%)	12 (11.7%)	13 (36.1%)	11 (30.5%)	1 (2.7%)
COPD	4 (3.9%)	3 (2.9%)	23 (22.5%)	19 (52.7%)	15 (41.6%)	-
Obesity	3 (2.9%)	5 (4.9%)	7 (6.8%)	7 (19.4%)	1 (2.7%)	-
Tumors	-	1 (0.9%)	3 (2.9%)	-	1 (2.7%)	-
Trauma	2 (1.9%)	-	-	6 (16.6%)	-	-
Surgery	3 (2.9%)	-	1 (0.9%)	2 (5.5%)	-	-
Oral contraceptives intake	4 (3.9%)	2 (1.9%)	-	-	-	-
Recurrent PE	-	1 (0.9%)	2 (1.9%)	20 (55.5%)	7 (19.4%)	1 (2.7%)

comparison with hemodynamic parameters of pulmonary circulation on admission and over time after therapy performed, we found maximal values of pressure in the trunk of pulmonary artery to be observed in patients with later hospitalization and thrombolytic therapy initiation. Besides, the dynamics of pulmonary pressure decrease after thrombolythic therapy were influenced first of all by the duration of phlebothrombosis history which determinates morphological features of thrombotic embolus, chronic bronchopulmonary and heart diseases (pressure in PC was initially higher in these patients) and recurrent thromboembolism (addition of fresh emboli). It was particularly evident in patients from group 1: in early admitted patients pulmonary pressure decreased to 25-29 mm Hg within one week after thrombolysis. It is related to morphological features of thrombotic emboli – they are less organized and more amenable to thrombolytic drugs influence. In patients with several risk factors such as phlebothrombosis history for over 3 months, CHF, COPD, recurrent PE, the pressure decreased to 36-38 mm Hg (Table 3).

In patients from group 2 with confirmed diagnosis of PE, in 12 months after the first episode the indices of pulmonary circulation were in linear dependence on the time of admission and made 84-86 mm Hg on the average, whereas the mean pressure decreased to 45-50 mm Hg. Major prognostic indicators for this group were recurrent PE and chronic thrombophlebitis (Table 3).

Analysis of clinical presentation of the disease in group 1 patients revealed that main complaints present on admission regressed and persisted in 38 (37.2%) patients, mainly as cough and minor dyspnea at physical exertion.

In group 2 significant regression of hemoptysis was seen in 5 patients (13.9%). Pain and cyanosis persisted in 13 (36.1%) and 11 (30.5%) patients, respectively, respectively, tachycardia persisted in 9 patients (25%). Dyspnea and cough almost did not regress and were present in 34 (94.4%) and 26 (72.2%) patients.

CONCLUSIONS

The diagnosis of clinical signs, treatment and prognosis of PE outcomes are still a challenge. We have followed the results of treatment at different time points from the moment of PE clinical signs manifestation till the initiation of TT.

We obtained convincing data concerning the influence of PE duration and such risk factors as phlebothrombosis, recurrent thromboembolism, CHF and COPD, on the degree of pulmonary pressure increase and the regression of clinical signs of pulmonary embolism. In patients with longer duration of the disease before treatment initiation (>1 month) severe increase of systolic pressure in the pulmonary arterial trunk and the right heart (65 mmHg) is noted. The decrease of systolic pressure in the pulmonary arterial trunk after thrombolythic therapy is less significant in this group and the pressure remained at the level of 44-50 mm Hg, while in patients with disease duration of 12 months it was almost not changed at all. Dyspnea, cough, tachycardia and decreased exercise tolerance persisted.

In patients hospitalized within the first week pulmonary systolic pressure returns to normal values (25-29 mmHg) after TT, clinical signs of PE also regress. In patients with risk factors such as phlebothrombosis of more than 3 months duration, recurrent PE, the pressure remains increased (36-38 mmHg), cough and dyspnea on physical exertion persist.

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Results of Primary PCI in STEMI Patients with Peripheral Artery Disease

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Immediate, in-hospital and long-term (up to 12 months) results of primary PCI in 259 STEMI patients (48 patients with manifestations PAD, 211 patients with coronary lesions only). Immediate angiographic success was achieved in the group of PAD in 45 (93,8%) patients, in the second group – in 205 (97,2%) patients, (p=0,468). Complete coronary revascularization was performed in 13 (27,3%) patients in PAD group and in 128 (66,6%) patients in the group with coronary lesions and without PAD (p=0,001). During in-hospital period the rate of MACE (death, stroke, non-fatal myocardial infarction, repeated revascularization of the target vessel) was not significantly different in the groups of study (10,4% and 7,6%, respectively; p=0,722). In 12 months the rate of MACE in PAD group was higher than in the group with coronary lesions only (37,5% and 18,9%, respectively; p=0,010). The difference was due to the increase of non-fatal MI frequency (20,8% and 9,0%, respectively; p=0,036).

Keywords: Peripheral artery disease, ST elevation mypcardial infarction, primary PCI.

Abbreviations:

PCI – percutaneous coronary intervention
AMI – acute myocardial infarction
STEMI – myocardial infarction with ST elevation
CA – coronary arteries
PAD – peripheral artery disease

INTRODUCTION

Cardiovascular diseases still are the main cause of death on the Earth. Thus, cardiovascular diseases account for over one half (55%) of all cases in the structure of general death (1).

The main cause of cardiovascular morbidity is atherosclerosis – a systemic disease involving several vascular systems. According to International REACH registry (2006) about 20% of patients with cerebral and lower limb ischemia have symptoms attributable to more than one vascular system (2).

The patients with peripheral artery disease (PAD) constitute the most complex category of patients, from the viewpoint of diagnostics as well as from the viewpoint of therapeutic point of view. The ischemic manifestations in one vascular region are often accompanied by latent or low-symptomatic course of atherosclerotic process in other vascular region, which can lead to fatal complications (3, 4). The 5-years survival in patients with atherosclerotic coronary lesions is about 70%, and survival of patients with isolated carotid lesion or lower limb lesion – about 80-85%. However in case of concomitant lesions of several vascular systems this index does not exceed 50% (5, 6).

The presence of PAD determines the baseline severity of the disease, complicates the choice of optimal tactics of management and puts in doubt the optimistic prognosis. This fact is of special importance for high-risk patients, in particular, for patients with myocardial infarction with ST elevation (STEMI). The results of numerous studies show that 15% of STEMI patients die already at pre-hospital stage, and without adequate myocardial revascularization another 12-15% of patients die in hospital. The performance of primary percutaneous coronary interventions (PCI) in STEMI patients has allowed for the decrease of in-hospital mortality to 5,9-7,5% (7, 8).

At present the management of PAD remains one of the main and still not completely solved problems of cardiovascular surgery (9). Up to now there are no data concerning the frequency of detection, clinical significance of concomitant PAD in patients with STEMI, concerning the results of endovascular interventions. All these complicate the treatment for this subset of patients.

PURPOSE OF STUDY

To evaluate early and long-term results of primary PCI in STEMI patients with concomitant peripheral artery disease.

MATERIAL AND METHODS

Retrospective registry comprised 259 subsequent patients who underwent primary PCI for STEMI. The duration of the follow-up was 12 months. After the determination of the diagnosis and the performance of a necessary minimum of diagnostic studies all patients were transferred to the cathlab for urgent coronary angiography (CAG) with subsequent PCI of the infarct-related artery (IRA). During hospital stay all patients underwent ultrasound examination of brachiocephalic vessels and lower limb arteries. The

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stenoses of more than 30% of non-coronary vessels were revealed in 33,6% (n=87) of patients, including significant lesions (stenoses > 50%) – in 18,5% (n=48) of patients (they were assigned to PAD group). All patients were divided into two groups: Group 1 (n=48) – patients with PAD (STEMI + PAD group), Group 2 (n=211) – patients without PAD (patients with coronary lesions only (STEMI group)).

Clinical characteristics of patients included in the study are shown in Table 1.

Patients in PAD group were older, among them there were more active smokers and more patients with previous MI.

The prevalence of atherosclerotic process in different vascular territories in STEMI + PAD group is shown in Table 2.

Anatomical characteristics of CA involvement were assessed using SYNTAX score, with higher score corresponding to more complex lesion of the CA. SYNTAX score of 22 and less corresponded to low degree of coronary lesions; SYNTAX score from 23 to 32 – to the degree, and score over 33 – to high degree of coronary bed lesion. Early (up to 30 days) and long-term (up to 12 months) results were evaluated using combined end-point – the rate of MACE (death from any cause, stroke, non-fatal MI and repeated target vessel revascularization). Besides we evaluated the frequency of repeated revascularization of non-target coronary vessel, the completeness of myocardial revascularization (indicating, whether the interventions were performed in all involved segments of the CA), the number of stents implanted per 1 patient and angiographic success of the intervention.

Statistical analysis was performed using the software package «BioStat 2007» ver. 3.8.4 (Analystsoft). The results are presented as means ± SD. The significance of the results' differences was evaluated using t-Student's and paired t-test (for parametric indices), qualitative comparison of the groups was performed using χ^2 test. The differences were judged significant at $p<0.05$.

RESULTS

Anatomical characteristics of the coronary lesions in the studied groups are shown in Table 3.

The severity of the coronary lesions, with SYNTAX score, as well as from the viewpoint of the number of affected vessels, was significantly higher in PAD group.

Immediate angiographic success was achieved in 45 (93,8%) patients in PAD group and in 205 (97,2%) patients in the group with coronary lesions only (p=0,468), the number of stents per 1 patient was 1,2 and 1,28, respectively (p=0,861). Complete myocardial revascularization was achieved in PAD group in 13 (27,3%), and in the group with coronary lesions only – in 128 (60,6%) patients, (p=0,001).

In-hospital and long-term results obtained in the studied groups are presented in Table 4.

In general, the rate of MACE during hospital stay was low and not statistically different between

Table 1. Cardiovascular risk factors for the studied patients.

Parameter	STEMI + PAD (n=48)	STEMI (n=211)	P
Age, years	61.5±8.11	57.0±8.98	0.001
Males	68.75% (33)	73.46% (155)	0.426
Diabetes mellitus	20.8% (10)	15.2% (32)	0.457
Arterial hypertension	93.75% (45)	88.2% (186)	0.384
Smoking	50% (24)	51.2% (108)	0.001
History of MI	33.3% (16)	11.4% (24)	0.001
History of ACVA	10.4% (5)	5.3% (11)	0.308
History of CABG, PCI	14.6% (7)	9.9% (21)	0.500

Table 2. Prevalence of atherosclerotic process in STEMI + MFA group (n=48).

Vascular territory		% (abs.)
CA + 1 vascular territory	Brachiocephalic arteries	20.8% (10)
	Lower limb arteries	60.4% (29)
CA + 2 vascular territories (brachiocephalic arteries + lower limb arteries)		18.8% (9)

Table 3. Characteristics of the coronary lesions.

Parameter	STEMI + PAD (n=48)	STEMI (n=211)	P
Syntax score	18.88±9.87	12.78±6.32	0.001
Syntax < 22	43.8% (21)	73.5% (155)	0.001
Syntax 22 - 32	41.7% (20)	25.1% (53)	0.034
Syntax > 32	14.6% (7)	1.4% (3)	0.001
1-vessel coronary lesion	29.2% (14)	61.2% (129)	0.001
2-vessels coronary lesion	50.0% (24)	27.1% (57)	0.003
3-vessels coronary lesion	20.8% (10)	11.8% (25)	0.159

Table 4. In-hospital and long-term results of primary PCI.

Parameter	STEMI + PAD (n=48)	STEMI (n=211)	P
In-hospital results (up to 30 days)			
MACE	10.4% (5)	7.6% (16)	0.722
Death	4.2% (2)	3.31% (7)	0.883
Stroke	0	0	-
Non-fatal MI	8.4% (4)	3.31% (7)	0.247
Repeated revascularization of the target vessel	2.1% (1)	0.9% (2)	0.933
Repeated revascularization of the non-target vessel	10.4% (5)	2.9% (6)	0.051
Cumulative indices in 12 months (including the data for the first 30 days)			
MACE	37.5% (18)	18.9% (40)	0.010
Death	8.3% (4)	6.2% (13)	0.821
Stroke	2% (1)	0.9% (2)	0.933
Non-fatal MI	20.8%. (10)	9% (19)	0.036
Repeated revascularization of the target vessel	6.25% (3)	2.8% (6)	0.468
Repeated revascularization of the non- target vessel	37.5% (18)	16.6%. (35)	0.002

the groups (the group with PAD and the group with coronary lesions only: 10,4% vs. 7,6%, p=0,722). The same rate for each of two unfavorable clinical outcomes – MI and stroke – included into the main index was noted in both groups. The frequency of repeated target vessel revascularization also was identical in both groups. The frequency of repeated interventions on non-target coronary vessel was higher in PAD group (10,4% vs. 2,9%, p=0,051). This was due to the severity of coronary lesions in PAD group which was significantly higher, and the rate of complete revascularization, which was significantly lower than in the group with coronary lesions only. During 12- months period the rate of MACE was significantly higher in PAD group in comparison with the second group (37,5% vs. 18,9%; p=0,010). The analysis of particular target outcomes showed that the rate of lethal complications, stroke, re-intervention on the target vessel was not different between the groups, while the rate of non-fatal MI was higher in PAD group than in the group with coronary lesions only (20,8% vs. 9,0%; p=0,036). The frequency of repeated revascularization of non-target coronary vessel also was significantly higher in PAD group and its cumulative rate at 12 months was 37,5% (p=0,002).

DISCUSSION

Our analysis is based on the comparison of early and long-term results of primary PCI in successively selected STEMI patients with or without PAD. The obtained results allow to say that primary PCI in patients with PAD is not accompanied by increasing risk of death and stroke, during the intervention and early post-procedural period as well as in the long-term.

Significantly higher rate of repeated revascularization of the target vessel seen within the first 30 days in patients with PAD was preserved after 12-months follow-up. In 1 year more cases of non-fatal MI were observed in PAD FA group, making significant the difference for cumulative MACE index between the groups. This can be explained by the differences in coronary lesions severity in the studied groups. Thus the evaluation of anatomical severity of coronary atherosclerosis using SYNTAX score revealed not only higher scores for PAD group, but also significantly higher frequency of severe coronary lesions. It is well known that the more severe and extensive is atherosclerotic process in CA, the higher is the probability of acute coronary syndrome development (10), and our results confirmed it. The anatomy of coronary lesions had an impact on the completeness of myocardial revascularization: this index was higher in the group with coronary lesions only. Probably, incomplete revascularization also contributed to a substantial increase of the rate of non-fatal MI during 12 months of the follow-up in PAD group. Our analysis allows to trace two eventual ways for the improvement of the results of endovascular interventions in STEMI patients with concomitant PAD:

1) complete myocardial revascularization in patients with PAD during primary PCI; 2) reduction of time interval before repeated intervention in non-target vessel.

CONCLUSIONS

1. The patients with PAD who underwent primary PCI in 56,3% of cases have severe or extremely severe (according to SYNTAX score) coronary lesions.
2. The severity of coronary lesions and incomplete myocardial revascularization (27,3%) in acute stage of STEMI in patients with PAD, probably, are the main causes of the increase of the rate of non-fatal myocardial infarction and of non-target vessel revascularization within the first 12 months after the primary PCI.

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Factors Influencing Surgical Prognosis in Patients with Aortic Valve and Coronary Artery Disease

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Moderate aortic valve stenosis is a common condition in patients with coronary heart disease (Gullinov and Garsia, 2005). Recent studies have shown that progression of aortic valve stenosis depends on the degree of valvular leaflets calcification; that aortic valve replacement does not increase mortality after coronary artery bypass grafting (CABG); moreover, valve replacement performed after CABG leads to decreased mortality, it was especially confirmed in patients with severe aortic valve stenosis. However, review of the literature concerning integration of the mathematical approaches in medicine has demonstrated that, the simple prognosis is more significant than an evaluation based on organ and system modeling for choice of treatment method and options for patients with such combined pathology. Repeated intervention is one of the most significant prognostic factors. Thus, after analyzing of 13,346 CABG cases Yap et al (2007) have shown that mortality of repeated interventions is approximately 3 times higher than that of primary interventions (4.8% and 1.8%, respectively). Patient's age is another such a factor. Urso et al. (2007) have established that one-year survival after aortic valve replacement in patients aged over 80 years (86,1%) is significantly less than that in the younger group. After analyzing of 1567 patients after valve replacement combined with CABG, Doenst et al.(2006) have demonstrated patients' gender influence on surgery outcomes, postoperatively women had higher stroke possibility (risk index was 1.52). We believe that various influences of parameters characterizing patient's baseline status on surgery outcome require more complex multivariate statistical analysis to be used. It allows to define rational number of the most significant factors determining the surgery prognosis related both to baseline status of patients with heart defects and immediate postoperative complications caused by interventional injury and heart hemodynamic changes (1, 2, 3, 4, 5, 6). Moreover, one of the authors of the article (Wann and Balkhy, 2009) considers that application of the most modern diagnostics tests (i.e. computed tomography coronary angiography) allows to predict an outcome of the scheduled surgery more accurately.

The objective of this study was to investigate factors affecting the outcomes of combined interventions performed in patients with aortic valve defects and coronary artery lesions and to evaluate anatomical and hemodynamic parameters influencing the prognosis.

MATERIAL AND METHODS OF THE STUDY

One hundred twenty eight (128) patients who underwent one-step aortic valve replacement and CABG were enrolled in the study (104 men and 24 women aged from 40 to 73, mean age was 56.4±1.5 years). Aortic valve stenosis was predominant in 82.8% (106) cases; aortic insufficiency was predominant in 17.2% (22) cases. Aortic valve lesions were caused by rheumatic process (65.6%), atherosclerotic degeneration and calcification (15.6%), and infective endocarditis (18.8%).

All patients underwent examination including chest X-ray, ECG, EchoCG. Increase in cardiothoracic index and change in pulmonary circulation were observed on X-ray scans. Enlargement of ascending aorta was revealed in all patients. Left ventricle hypertrophy and intraventricular conduction disturbance were observed on ECG. Aortic valve defect was complicated by valvular and extravalvular calcification in 87.1% patients: 3.2% - Grade I, 22.6% -Grade II, 32.3% - Grade III, 29% - Grade IV, absolutely, it was a complicating factor for surgery.

Table 1 presents the distribution of patients by chronic heart failure (CHF) and New York Heart Association Functional Class (NYHA FC).

Table 1. Distribution by chronic heath failure stage and functional class.

NYHA Functional Class	Number of patients	HF	Number of patients
II	21 (16.1%)	IIA	88 (68.7%)
III	78 (61.3%)	IIБ	40 (31.3%)
IV	29 (22.6%)		

All patients were operated using cardiopulmonary bypass and cardioplegia. Mean time of cardiopulmonary bypass was 178.5±7.8 min, time of aortic occlusion was 132.8±5.0 min. One hundred eight (108) mechanical (75 bicuspid, 33 unicuspid) and 20 biological prostheses were implanted. The most common aortic valve prostheses were MEDINZH, SorinBicarbon, EMIKS, KEM-AV-MONO, KEM-AV-COMPOZIT.

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All patients who had significant coronary artery lesions (stenosis >50%) underwent coronary artery bypass grafting: one artery – in 56 (43.8%) patients, two arteries – in 42 (32.8%) patients, three arteries – in 30 (23.4%) patients. Concomitant mitral and tricuspid insufficiency was corrected in 25 and 23 patients, respectively. Atrioventricular valve insufficiency was in all cases caused by fibrous annulus dilatation, which was treated with support ring implantation.

Patient status at baseline was a landmark to determine all totality of defect pathogenetic disorders, and evaluation of the factors affecting the separate components of complete clinical picture creation permitted to consider specially the causes, conditions and consequences of systemic positions. Calculations were performed using «STATISTICA for Windows», v.6.0 and original programs developed in "Excel - 2000" on "Visual Basic for Application" integrated computer language. Group data were divided into numeral and classification ones; additional tables for deviations (abs. and %) of variables from baseline levels were calculated. Difference significance was evaluated by χ^2 criterion, and 2x2 tables by adjusted Fisher test.

Distribution parameters were evaluated by formulas as follows:

$$\mathbf{M}=\frac{1}{N}\sum_{i=1}^{n} X_i;\quad \mathbf{S}=\sqrt{\frac{1}{N-1}\sum_{i=1}^{n}}\ (X_i-\mathbf{M})^2;\quad \mathbf{m}=\mathbf{M}\frac{S}{\sqrt{N}}$$

Consistency of numerical data with normal distribution law was assessed with Kolmogorov test. If the numerical data did not correspond to normal distribution law, non-parametric statistical methods were used - Wilcoxon rank test. Power and direction of correlation between the signs were determined by Pearson correlation coefficient **(r)** and Spearman rank correlation, if distribution of the baseline data was not normal. The values of these tests range from -1 to +1. The extreme values are observed in signs associated with linear functional relation. The significance of selected correlation coefficient is assessed by statistics value $r^*\sqrt{n-2}/\sqrt{1-r2}=t_{a,f}$ (1). Expression (1) permits to determine a, i.e. possibility of correlation coefficient difference from zero depending on r and sample size n. This, in turn, allows to compare the correlation of the same signs in the different sample sizes by possibility. Correlation power was assessed by a value of the correlation coefficient: strong, if r ⩾0.7, moderate, if r = 0.3-0.7, weak, if r<0.3. The differences between compared values were significant if p<0.5, it is consistent with criteria accepted in medical and biological researches.

Prognosis model is based on the regression analysis. Regression analysis was directed to the test of significance of one (dependent) variable Y from set of other ones, so called independent variables Xj = {X1, X2, ... Xp}. The values of the prognostic parameter are defined as a result of determination of the risk factors based on analysis of the clinical materials. The purpose of linear regression analysis in this study was to predict the values of the resulted variable Y using the known values of physical parameters, EchoCG parameters and various additional features related to surgery specificity. Parameter of favorable surgery outcome was calculated as an arithmetic mean of risk factors. As a result of these calculations, the model was developed. Based on this model the program was created in “Excel–2000»: «Program for outcome prognosis of aortic valve replacement combined with coronary heart disease» (CERTIFICATE ГПВ РУз № DGU 01380») allowing to calculate a percentage of favorable surgery outcome and dynamics of LV ejection fraction after a surgery with prognostic significance 75-90%.

RESULTS AND DISCUSSION

As a result of the performed analysis the variables pooled in factor groups **(F)** affecting the surgery prognosis were determined: **F1** – blood supply disturbance (HF, NYHA FC), **F2** – physical parameters (gender, age*, weight*, height*, body surface area*, Ketle index*, CTI*), **F3** – hemodynamic parameters (SBP*, DBP*, MBP*, BSV, HR*, BMV*, TPR*, SPR, HI*, LV stroke work*), **F4** – heart parameters (EDD*, ESD*, EDV*, ESV*, SV*, EF*, FS*, RF*, SVE*, RV*, LA*, RA*, PA*), **F5** – myocardial parameters (IVS*, LVPW*, LVMM*, sPLVWT and dPLVWT*, 2HD*), **F6** – valve morphology (calcification degree on AV, regurgitation degree on AV, MV, and TV), **F7** – valve parameters (FA and ascending aorta diameter*, AV gradients*, AO* surface, MO* surface, MV gradients*, Emv, Amv, E/A mv), **F8** – coronary blood supply parameters (blood supply type, percentage of coronary artery occlusion (LAD, DB, CA, RCA), number of planned bypass grafting). Indexed parameters, reverse values and second degree were considered in «*» variables, it has been leading to increase in prognosis efficacy (see Table 2).

We determined that a percentage of complex factor influence on surgery prognosis – peak systolic gradient (PSG) and post-operation ejection fraction dynamics were different (Diagram 1).

Diagram 1. Percentage of complex factor influence on prognosis, PSG, LVEF in patients suffered from valve defect combined with coronary artery lesions.

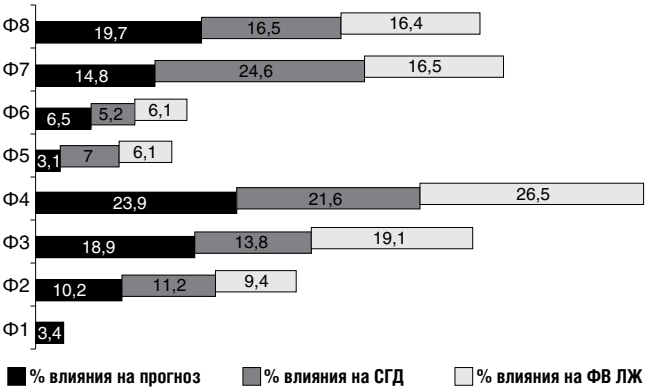


Table 2. Risk factors and variables and its components.

№	Variable	Unit	Definition	Variable nomenclature
I Blood supply disturbance (F1)				
1	HF		I, IIA, IIB, III	Heart failure
2	FC		I, II, III, IV	Functional class
II Physical parameters (F2)				
1	Gender		1 - man, 2 – woman	Patient gender
2	Age*	years		Age
3	Weight*	kg		Weight
4	Height*	cm		Height
5	BSA*	m^2	BSA = 0.007184 * Weight^0.423 * Height^0.725	Body surface area
6	Ketle index*	U	Ketle index = 10000* Weight/Height^2	Ketle index (body weight index)
7	CTI*	%		Cardiothoracic index
III Central hemodynamic parameters (F3)				
1	SBP*	mmHg		Systolic blood pressure
2	DBP*	mmHg		Diastolic blood pressure
3	MBP*	mmHg	MBP = DBP+((SBP - DBP)/3)	Mean blood pressure
4	PBP*	mmHg	SBP-DBP	Pulse blood pressure
5	BSV		BSV = 90.97 + 0.54 * PBP– 0.57 * DBP – 0.61*Age	Blood stroke volume by Starr (39)
6	HR*	beat per minute		Heart rate
7	CO*	l/min	CO= SV * HR / 1000	Cardiac output (blood supply)
8	TPR*	dyne*cm-5	TPR=79.92*MBP/CO	Total peripheral resistance (59)
9	RPR		RPR=TPR/BSA	Relative peripheral resistance (110)
10	HI*	U	HI=CO/BSA	Heart index (109)
11	Asw*	U	Asw(LV) = SV*1.055*(MBP-5)*0.0136	LV stroke work (153)
12	LVMW	U	LVMW=0.0136*1.055*CO*(MBP-5)	LV minute work (157)
13	LVWI		LVWI=0.0136*1.055*HI*(MBP-5)	LV work index (160)
14	LVWSI		LVWSI=0.0136*1.055*SI*(MBP-5)	LV work stroke index (161)
15	HFi		HFi=SBP*HR/LVMM	Heart functioning index
IV Heart parameters (F4)				
1	EDD*	cm		End-diastolic dimension
2	ESD*	cm		End-systolic dimension
3	EDV*	cm^3	EDV=7*EDD^3 / (2.4+EDD)	End-diastolic volume
4	ESV*	cm^3	ESV=7*ESD^3/(2.4+ESD)	End-systolic volume
5	SV*	cm^3	SV=EDV-ESV	Stroke volume
6	SI*	U	SI=SV/BSA	Stroke index (108)
7	LVEF*	%	LVEF=100*(EDV-ESV)/EDV	Ejection fraction
8	LVFS*	%	LVSF = 100*(EDD-ESD)/EDD	Fractional shortening
9	RF	%	RF=ESV/EDV*100	Residual fraction (55)
10	SVE	%	SVE=100*EDV/ESV*100	Systolic ventricular ejection (56)
11			КР = (КДО-КСО)/(КДД-КСД)*1/КСО	коэффициент растяжимости стенки
12	TC*		TC = (EDV-ESV)/(EDD-ESD)*1/EDV	Ventricular wall tensility coefficient (57)
13	LA*	cm		Left atrium
14	RA*	cm		Right atrium
15	PA*	cm		Pulmonary artery
16	PAP	mmHg		Pulmonary artery pressure
17	PA FAD	mm		PA fibrous annulus diameter
V Myocardial function parameters (F5)				
1	dIVST*	cm		Diastolic interventricular septum thickness
2	dPLWT*	cm		Diastolic posterior LV wall thickness
3	LVMM*	g	LVMM=1.04*((EDD+IVS+IVS)^3 - EDD^3)-13.6	LV myocardial mass
4	rsPLWT*	U	rsPLWT=dPLWT/EDD	Relative systolic posterior LV wall thickness
5	rdPLWT*	U	rdPLWT=dPLWT/ESD	Relative diastolic posterior LV wall thickness
6	2HD*	U	2HD = (dPLWT+dIVST)/EDD	Relative double thickness

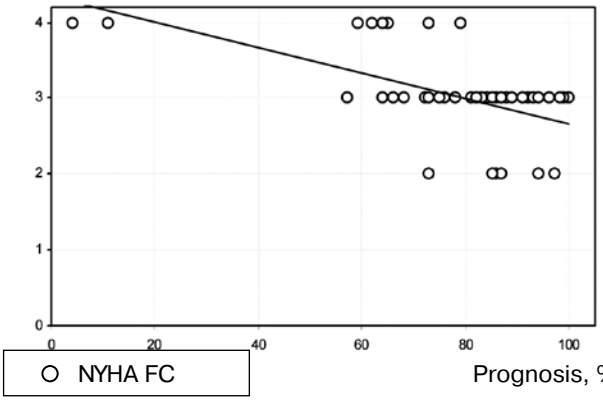
№	Variable	Unit	Definition	Variable nomenclature
VI Valve morphology (F6)				
1	AVca	score	1,2,3,4	AV calcification, degree
2	AVreg	score	1,2,3,4	AV regurgitation, degree
3	MVreg	score	1,2,3,4	MV regurgitation, degree
4	TVreg	score	1,2,3,4	TV regurgitation, degree
V Valve function parameters (F7)				
1	ARD*	cm		Aortic root diameter
2	AAD*	cm		Ascending aorta diameter
3	AVppg*	mmHg		AV peak pressure gradient
4	AVmpg*	mmHg		AV mean pressure gradient
5	AVsfs	m/s		AV systolic flow speed
6	AOs*	cm2		Aortic orifice surface area
7	Emv			MV E peak
8	Amv			MV A peak
9	E/A mv	U	E/A mv = E mv / A mv	E/A ratio
10	MOs*	cm^2		Mitral orifice surface area
11	MVppg	mmHg		MV peak pressure gradient
12	MVmpg	mmHg		MV mean pressure gradient
VIII Coronary blood supply parameters (F8)				
1	CVG		1 – right, 2 – balanced, 3 - left	Blood supply type by CVG
2	LAD	%		Left anterior descending, lesion %
3	DB	%		Diagonal branch, lesion %
4	CA	%		Circumflex artery, lesion %
5	RCA	%		Right coronary artery, lesion %
6	IA	%		Intermediate artery, lesion %
7	No. of grafts	pcs		Number of grafts

Thus, heart parameters (F4) (r=0.320 p<0.01), coronary blood supply parameters (F8) (r=0.165 p<0.05), F3 (r=0.330 p<0.01), valve function parameters (F7) (r=0.183 p<0.05), and physical parameters (F2) (r=0.223 p<0.05) had greater influence on prognosis. However, valve functions (F7) (r=0.320 p<0.01), heart parameters (F4) (r=0.261 p<0.05), coronary blood supply parameters (F8) (r=0.046 p<0.05), hemodynamic parameters (F3) (r=0.284 p<0,05), and myocardial function parameters (F5) (r=0.589 p<0.001) have played greater role for peak systolic gradient (PSG). The parameters of the following factors affect changes in LV ejection fraction: heart parameters (F4) (r=0.381 p<0.01), hemodynamic parameters (F3) (r=0.332 p<0.01), coronary blood supply parameters (F8) (r=0.322 p<0.01), and valve function parameters (F7) (r=0.332 p<0.01).

The positive surgery prognosis in patients with lower HF (r=-0.111) and lower NYHA FC (II, III) (r=-0.560) was higher than 80%. However, in operated patients with FC IV the surgery prognosis was less than 80%. It was noted that higher FC corresponded to lower LV EF values (r=-0.086). It means that FC IV is a high risk predictor for combined surgeries (Diagram 2).

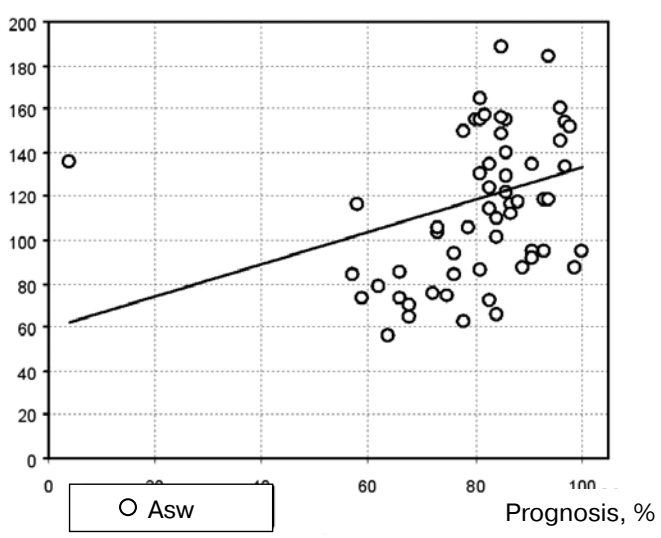
Physical parameters (F2) suggested that PSG on AV had a trend to increase with age (r=0.264), i.e. compensated processes are progressing depending on age, although general biological and physiological processes are decreasing. However, age had no significant influence on surgery prognosis (r=-0.162).

Diagram 2. Correlation between prognosis and functional class.



Moderate correlation between prognosis (r>0.31) and peak SPG (r>0,206) was observed when hemodynamic parameters were analyzed (F3). The correlation was direct for prognosis and reverse for SPG: e.g. in patients with CO more than 4.0 l/min surgery prognosis was higher. This parameter increased not due to HR, but due to minute volume (r=-0.215). Such pattern was observed between parameters of LV stroke work (Asw): surgery prognosis was higher if LV Asw was higher (r=0.468). But if SPG was increased, decrease in LV Asw was observed (r=-0.295). It may be concluded that increase in afterload leads to decrease in LV work efficacy (Diagram 3).

Diagram 3. Correlation between prognosis with SPG and LV stroke work.



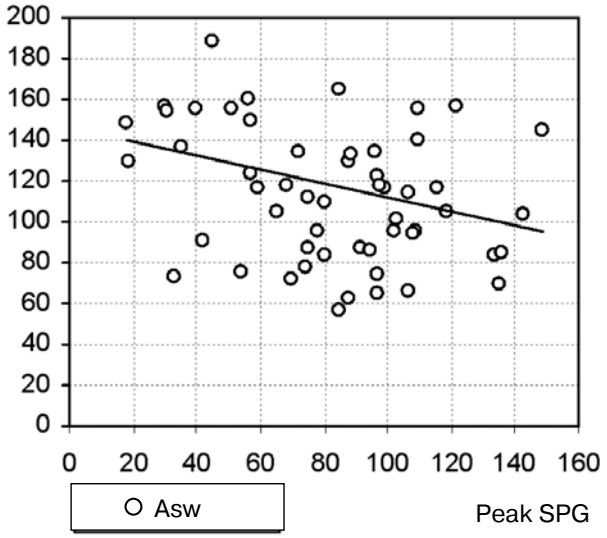


Diagram 4. Correlation between SV and SI with surgery outcome.

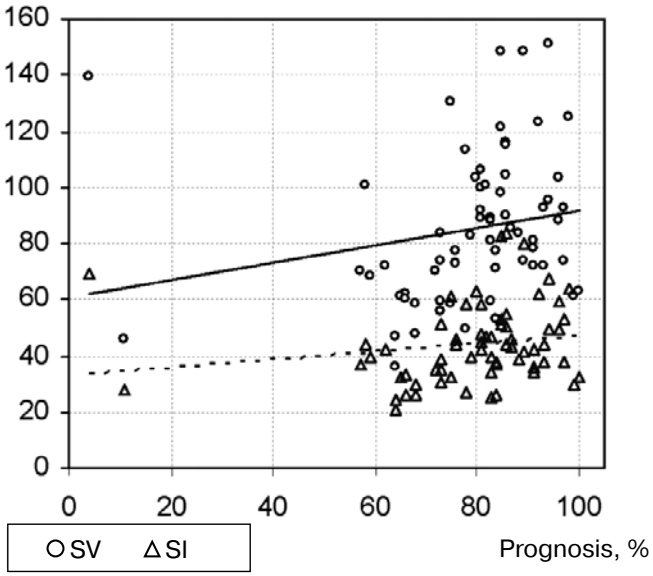


Diagram 5. Influence of EDV and ESV on LV ejection fraction.

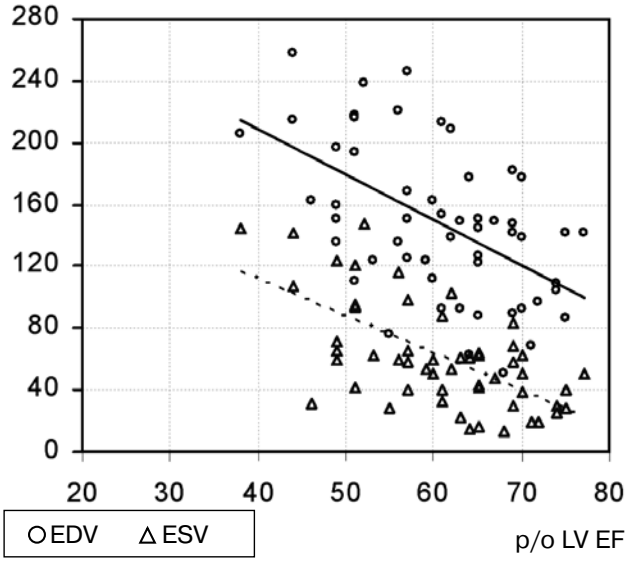


Diagram 6. Influence of baseline EDV and ESV on calculated LV EF.

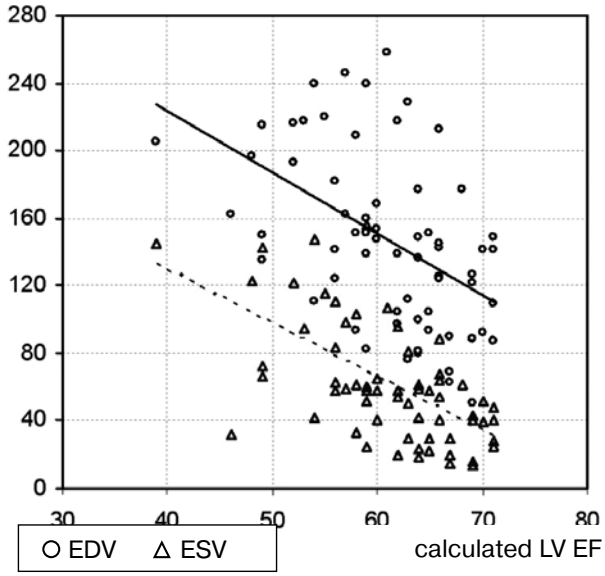


Diagram 5. Influence of EDV and ESV on LV ejection fraction.

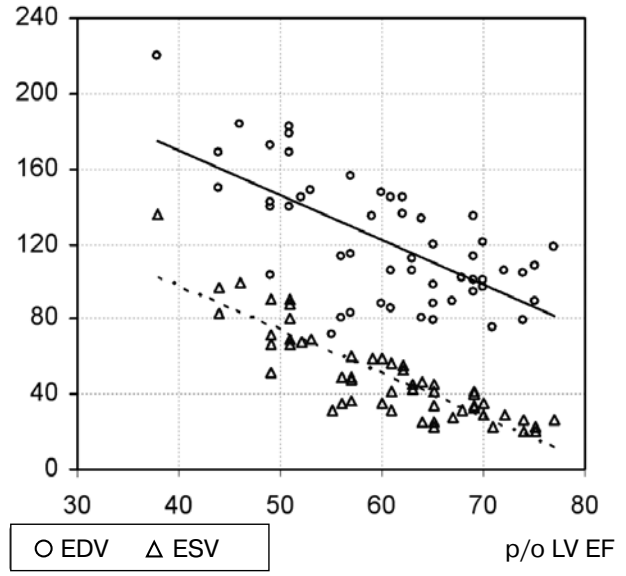


Diagram 7. Correlation of calculated LV EF with pre- and postoperative LV EF.

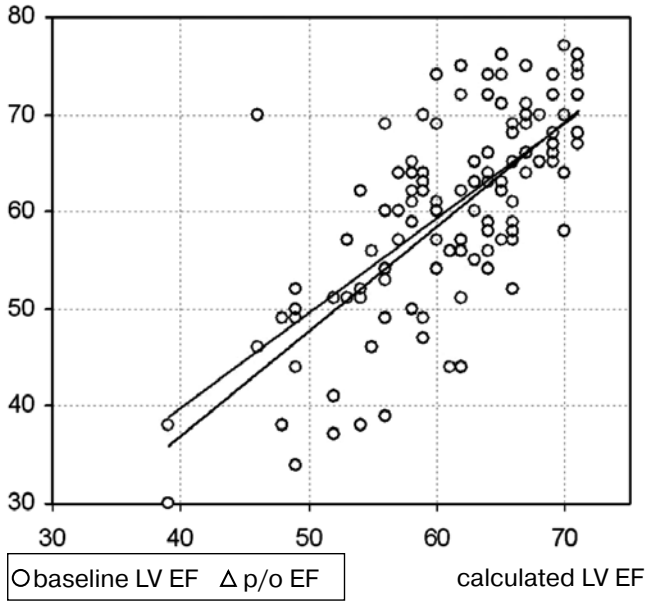
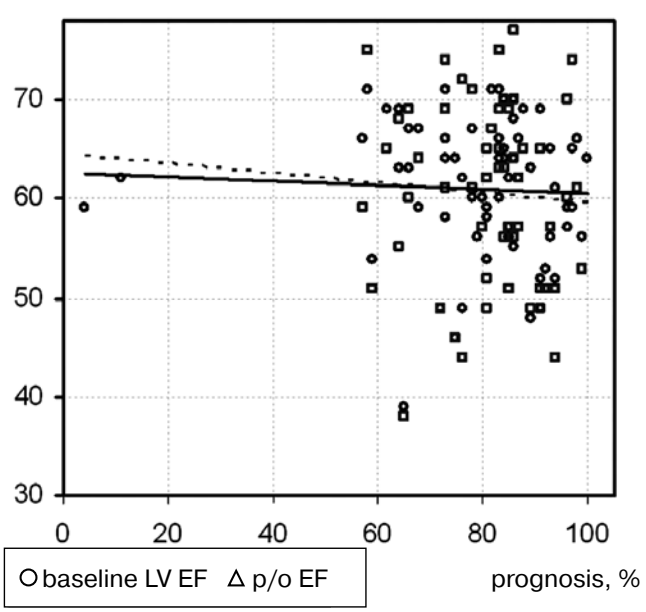


Diagram 8. Correlation between postoperative EF and calculated LV EF.



If peak SPG is more than 60 mmHg, LV Asw becomes less than 100 U, and favorable surgery prognosis does not exceed 80%. If stroke work was more than 100 U, positive surgery prognosis was 80-100%. It means that in patients with coronary artery lesions in combination with aortic defect SPG ⩾ 60 mmHg is one of indications for aortic valve replacement.

Heart parameters (F4) had the greatest influence on surgery prognosis. Thus, LV parameters had direct correlation with prognosis (r>0.224) and LV EF dynamics (r> 0.598) and reverse correlation with SPG (r<-0.343). LV end-diastolic dimension (EDD) and end-diastolic volume (EDV) had a greater influence on prognosis (r=0.349 and r=0.429, respectively), than LV end-systolic dimension (ESD) and end-systolic volume (ESV) (r=0.303 and r=0.352, respectively). Even in cases when increase in LV EDD (EDV) was observed after surgery and LV ESD (ESV) was constant (or decreased), possibility of favorable surgery prognosis was increased. This relationship between EDV and ESV contributes to increase in stroke volume (SV) and suggests preservation of LV myocardial contraction. The analysis showed that increased SV (r=0.458) and stroke index (SI) (r=0.385) was associated with increased percentage of favorable prognosis. We have found that if SI was >40 ml/m^2 (SV=80 ml), positive surgery prognosis was more than 80% (Diagram 4).

Analysis of influence of baseline EDV and ESV on postoperative LV EF has shown that this value was greater in patients with preserved LV parameters, and in patients with significant reduction of LV EDV and ESV (Diagram 5).

The performed analysis revealed that in patients with normal LV myocardial contractility at baseline we had good prognosis and increased LV EF after surgery. It was determined that if LV EF is higher than 50% at baseline, the positive surgery prognosis exceeds 80%. Such pattern of baseline EDV and ESV influence on LV EF dynamics was observed, if LV EF parameters obtained from calculation using the program for prognosis were analyzed. (Diagram 6).

LV EF calculated using the program for prognosis significantly correlated with true numbers of baseline and postoperative LV EF (Diagram 7).

Assessment of correlation between postoperative LV EF parameters and calculated ones using the program for surgery prognosis revealed a common pattern (trend lines had similar direction of dynamics and were approximately at the same level) (Diagram 8).

Decrease in postoperative LV EF is caused by cardiopulmonary bypass, aortic occlusion, and cardioplegia through unfavorable influence on myocardial contractility in spite of coronary artery bypass grafting, procedure improving coronary blood supply, activation of hibernated myocyte.

Analysis of myocardial function parameters (F5) showed that surgery prognosis is highly affected by posterior left ventricular wall thickness (PLVWT) (r=-0.306) and to lesser extent by interventricular septum thickness (IVST) (r=-0.072). Increase in IVST leads to greater increase in peak SPG rather than PLVWT (r=0.679 and r=0.526, respectively). It can be possibly explained by appearance of additional component of LV outflow tract obstruction as a hypertrophied IVS. When thickness of IVC and PLVW ranges from 1.5 to 2.0 cm, SPG is equal to 80-120 mmHg, and positive surgery prognosis is 80-100%. However, increased dimensions of IVS and PLVW lead to decrease in percentage of favorable prognosis. Degree of ejection fraction increase was mostly related to PLVWT (r=0.433) than to IVST (r=0.265), had no relation with LV myocardial mass (r=-0.113), although increase in myocardial mass improved surgery prognosis. Thus, optimal left ventricle myocardial mass (LVMM) value was 350-600 g (200-400 g/m^2) in the presence of corresponding linear parameters of LV and IVS. In these cases, positive surgery prognosis was more than 80%. Increase in ejection fraction more

than 50% was postoperatively observed especially in patients with such characteristics.

Analysis of valve morphology parameters (F6) revealed that significance of aortic valve calcification increases in peak SPG (r=0.448), but not affecting surgery prognosis (r=0.172). Baseline AV regurgitation also does not influence on surgery outcome (r=0.263). We can see, the possible explanation of this fact is that AV calcification in the patients was mostly caused by age-related sclerosis and rheumatoid degeneration with no elements of myocardial inflammation (myocarditis) and inflammation of conduction system.

Decreased ejection fraction was observed in patients who had regurgitation on MV (r=-0.377) and TV (r=-0.313) exceeding Grade I, this also resulted in impairment of surgery prognosis.

Analysis of valve function parameters (F7) demonstrated that lower baseline SBG value was associated with more favorable surgery prognosis (r=-0.284). When peak SPG was less than 80 mmHg, favorable surgery prognosis ranged from 90 to 100%. Therefore, in the patients with coronary artery lesions aortic valve replacement should be performed at the early stages of defect manifestations when a systolic gradient is 60-80 mmHg.

Analysis of coronary blood supply factor (F8) showed that patients with right dominance had worse surgery prognosis than patients with left dominance. Analysis demonstrated that among patients with right dominance only one artery was grafted in 41.9% patients, and 58.1% patients had two grafted arteries (35.5%) or more (22.6%). However, among patients with left dominance, one artery was grafted in 66.7% patients and only 33.3% patients had two (22.2%) or more (11.1%) grafted arteries, i.e. we see that the larger grafting volume was performed in patients with right dominance. Thus, greater number of grafts required corresponds to worse surgery prognosis (r=-0.312). Analysis of coronary artery lesions showed that significance of left descending artery (LAD) lesions, i.e. necessity of its grafting makes worse surgery prognosis (r=-0.303). It was also revealed that there is a direct correlation between grade of LAD lesion and value of mitral regurgitation (r=0.283). This suggests a significant role of LAD in coronary blood supply and it should be grafted if affected, especially in patents with combined lesion of aortic valve and coronary arteries.

Our conclusions generally support the literature data. Analysis of the huge body of materials (108 687 aortic valve replacements) performed by Brown et al. in 2009 demonstrated that female gender, age above 70 years and ejection fraction less than 30% led to higher postoperative mortality, higher percentage of postoperative stroke, and prolonged duration of hospitalization. The authors confirmed the data published by Doenst et al. in 2006 on higher incidence of stroke in women during immediate postoperative period, and did not confirmed the data on a similar percentage of mortality. Although, Doenst et al. (2006) analyzed cases of combined CABG and valve replacement (1567 patients). But this also cannot be a final conclusion (combined interventions have worse results than that of one-organ surgeries). However, Thulin and Sjogren (2000) did not demonstrate any differences in the results of simple aortic valve replacement (121 patients) and valve replacement in combination with CABG (98 patients). Some investigators apart from hemodynamic parameters pay attention on the values of laboratory tests. Thus, Florath et al. (2006) showed that elevated blood levels of glucose, creatine kinase, lactate dehydrogenase, sodium, and proteins in patients prior to aortic valve replacement and CABG (908 patients) resulted in increased postoperative mortality. Jamieson et al. demonstrated results similar to our ones (2003). Bioprosthetic valve replacement and CABG was performed in 1388 patients. The mortality rate in NYHA I-II and NYHA IV was 2% and 16%, respectively. The mortality rate in men and women was 4.6% and 13.8%, respectively. Older patients more often required repeated interventions (59 versus 52 years). Nardi et al (2009) showed that surgery prognosis was worse in patients with low ejection fraction, history of paroxysmal ventricular tachycardia, renal insufficiency, and anterior myocardial infarction prior to surgery.

CONCLUSION

Patients with aortic valve lesion combined with coronary artery lesion are a severe group for surgical treatment and require intervention at early stages of the disease. NYHA FC IV is a high-risk predictor for combined surgeries CHD + CABG. We believe that systolic gradient ⩾60 mmHg in patients assigned to CABG is an indication for combined aortic valve surgery. Analysis of LV linear and volume parameters revealed that LV diastolic dimension and diastolic volume had the greatest influence on prognosis in this patient group. iEDV/iESV ratio with SI>40 ml/m2 (SV=80 ml) is a good prognostic sign allowing to predict a prognosis of more than 80%. The optimal LVMM value was 350-600 g (200-400 g/m2) in the presence of corresponding linear parameters of LV and IVS, when a surgery prognosis was higher than 80%, and baseline LVEF was more than 50%. Appearance of functional changes in MV (regurgitation grade >1) and TV (regurgitation grade >1) is a poor prognostic factor. LAD grafting in these patients is a required intervention, even is a lesion degree is less than 70%. It allows to increase the favorable surgery percentage.

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Age-Related Aspects of Cardiospecific Autoantibodies Levels in Children with Arrhythmias

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Keywords: heart rhythm and conduction disturbances, myocardium, cardiospecific autoantibodies, myocardial cytoplasmic antigens, membrane/cytoskeleton antigens, β1-adrenoreceptors

The clinical, instrumental and immunological examinations were performed in 77 children of three age groups with heart rhythm and conduction disturbances (CRCD): group I - 18 children aged from 2 to 6 years; group II - 21 children aged from 7 to 10 years; group III - 38 children aged from 11 to 16 years. The serum levels of IgG class autoantibodies to certain cardiac antigens were determined in all patients. Multidirectional abnormalities in production/serum levels of cardiospecific autoantibodies were revealed which indirectly confirmed the etiological and pathogenic heterogeneity of arrhythmias. In general, without considering the age of children with arrhythmias, the most typical abnormality was the abnormally low serum levels of cardiospecific autoantibodies, suggesting impaired elimination of natural catabolic products. The autoantibodies to a soluble cytoplasmatic antigen predominantly responsible for development of functional and metabolic changes in myocardium predominated among overproduced antibodies revealed in one-quarter of HRCD patients. The overproduction of anti-cardiac autoantibodies, which was often polyspecific, was most typical for children of early and preschool age. This may suggest a recently developed immuno-inflammatory process in the myocardium and autoimmune genesis of arrhythmia in this age group, and supports the indication for anti-inflammatory therapy.

Abbreviations

Auto-Abs – autoantibodies
HRCD – rhythm and conduction disturbances
COS-05 – soluble anionic cytoplasmatic antigen of myocardiocytes
COM-02 – membrane/cytoskeleton antigen of myocardiocytes
Myocardial β1 – adrenoreceptors – β_1AR
NOS – NO-synthase antigen
ELISA – enzyme-linked immunosorbent assay

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The damage of cardiac structures by different factors, in particular, viruses which initiate the immuno-inflammatory (autoimmune) process in myocardium is currently considered to be one of the reasons leading to heart rhythm and conduction disturbances (1, 2). In some patients, the myocarditis has an indolent nature and clinically asymptomatic course, and arrhythmia is often considered as idiopathic (3).

At the molecular level, development of any disease leads to impaired synthesis and degradation of organ cellular structures resulting in changes in production of organ specific antibodies (auto-Abs), which are synthesized in human body throughout life starting from intrauterine period with rather specific individual quantitative variations. It has been suggested that such auto-Abs participate in clearance of natural catabolism products from the body and in the regulation of multiple physiological functions. (4, 5, 6).

Anti-myocardial antibodies to different cardiac antigens, when risen up to pathological values, may be either "witnesses"» of the development of pathological process in myocardium or the reason of it (7, 8, 9, 10).

The indirect evidence of hypothesis that auto-Abs are related to heart rhythm and conduction disturbances is the increased concentration of immunoglobulins A and G along with immunoregulatory imbalance of T- and B lymphocytes in patients with arrhythmias (11, 12). Clinically significant titers of anti-cardiac antibodies against the heart conduction system are observed in children with high-grade sick sinus syndrome (13). The increased levels of circulating auto-Abs, mainly to collagen and elastin, are reported in children with connective tissue dysplasia syndrome having arrhythmia (14). Auto-Abs to nerve growth factor and auto-Abs to β1-adrenoreceptors are the established immunological markers of electric myocardial instability (2, 8).

However, it should be noted that overproduction of auto-Abs of various organ specificity may be the secondary adaptive (sanogenous) response of immune system, induced by primary infectious, toxic or other organ impairment. This secondary rise in the auto-Abs synthesis provides the increased clearance of impaired organ from toxic catabolites, particularly, from products of accelerated apoptosis of its elements, and stimulates the regeneration as well. The abnormally low levels of auto-Abs may suggest the impaired elimination of natural catabolic products (6).

No matter our views about the role of auto-Abs in pathogenesis of different diseases ("witnesses", protectors, aggressors), it is obvious that abnormal

changes in serum auto-Abs levels are the markers of emerging (or existing) pathological process in the body. It is supported by the literature data on the diagnostic, differential diagnostic, clinically modifying and prognostic value of organ specific auto-Abs levels in patients (including children) with diabetes mellitus, pyelonephritis and nervous system disorders (15, 16).

One of the features of HRCD in children is the absence of subjective feelings indicative of the arrhythmia presence. The lower the children age, the more rare the complaints and arrhythmias are documented. The first detection of HRCD in school, prepuberty or puberty age often makes impossible the determination of arrhythmia duration. It may only be presumed that heart rhythm disturbances are often revealed in the eng of the pathological process, rather than in the beginning of it.

The purpose of this study was the investigation of age-related aspects of cardiospecific autoantibodies levels in children with arrhythmias.

MATERIAL AND METHODS OF THE STUDY

Seventy seven children have been investigated aged from 2 to 16 years (group I - 18 children aged from 2 to 6 years; group II - 21 children aged from 7 to 10 years; group III - 38 children aged from 11 to 16 years) with various types of HRCD: a) tachyarrhythmias (n = 13), including 5 children with chronic non-paroxysmal tachycardia and 8 children with paroxysmal tachycardia; b) extrasystoles (n = 25); c) I-II type sick sinus syndrome (n = 17); d) complete block of the right bundle branch (n = 5); e) prolonged QT interval syndrome (n = 6); f) I-III degree AV-block (n = 7); g) chronic sinus tachycardia (n = 3); h) atrial flutter (n = 1). Analysis of correlation between cardiospecific autoantibodies levels and the character of arrhythmia was not performed in this study.

In addition to routine methods using clinical and historical findings and instrumental investigations, the immunochemical tests were performed. The levels of IG class auto-Abs to soluble cytoplasmatic antigen of myocardiocytes COS-05, membrane/cytoskeleton antigen of myocardiocytes COM-02, cardiac β1-adrenoreceptors(β_1AR) and NO-synthase antigen (NOS) involved in vessel tonus regulation were determined. The tests were performed using enzyme linked immunosorbent assay (ELISA) with standardized test-systems ELI-TEST (manufacturer - MIC "Immunculus", Russia) according to manufacturer's instruction. The normal level of serum immunoreactivity in children of early preschool age was considered to be within the range from -40 to -10 conventional units (with any of antigens), in children of early school age – from -40 to 0 conventional units, and in children of school age – from -30 to +10 conventional units (Poletaev, 2008). The individual results below the lower limit of normal were considered as abnormal decrease of the respective serum auto-Abs levels; the results above the upper limit of normal were considered as abnormal increase of the respective serum auto-Abs level.

RESULTS OF THE STUDY

Investigation of children with HRCD revealed the overproduction of auto-Abs in 19 (24.7%) patients and the reduced production – in 50 (64.9%) children. Multidirectional shifts (combined overproduction of certain auto-Abs and low production of other auto-Abs) were revealed in 4 (5.2%) children. The normal values of all auto-Abs were also documented in 4 (5.2%) children.

Most commonly the overproduction was seen for the autoantibodies to soluble cytoplasmatic myocardial proteins COS-05 (20.7%), M±m = 17.8 ± 6.7 conventional units and β_1AR (15.6%), M±m = 7.8 ± 6.0 conventional units (Fig.1). The increased levels of antibodies to myocardial membrane proteins CoM-02 (6.5%) and NO-synthase were rarely observed (3.9%). Combined increase in auto-Abs to soluble cytoplasmatic myocardial proteins and β1-adrenoreceptors was observed most often.

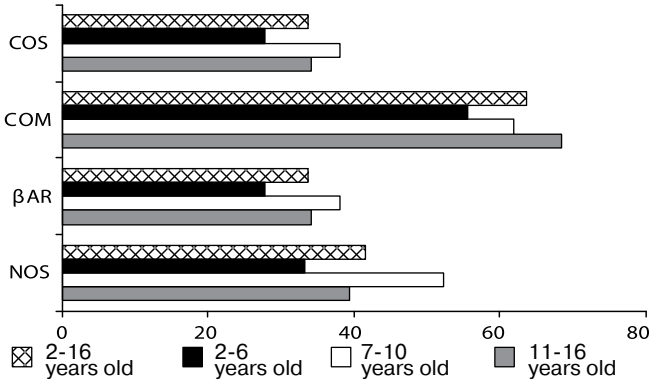

Figure 1. The structure of auto-Abs overproduction in children with HRCD by age.

The reduced production (Fig.2) was more frequently observed for antibodies to myocardial membrane proteins COM-02 (63.6%), M± = 53.1±2.6 conventional units. The decrease in levels of other auto-Abs were rarely observed and ranged from 32.5% (auto-Abs to COS-05 antigens) to 37.7% (auto-Abs to NOS).

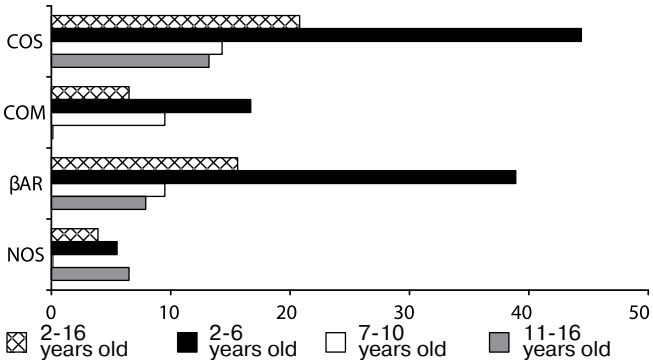

Figure 1. The structure of reduced auto-Abs production in children with HRCD by age.

The analysis of cardiospecific autoantibodies levels in children with arrhythmia demonstrated that overproduction of auto-Abs was most often observed in patients aged 2-6 years (group I – 44.4%) com-

Table 1. The incidence of cardiospecific autoantibodies overproduction in children with arrhythmia in different age groups.

Children groups	Abs overproduction	Combined Abs overproduction
Group I (n=18)	44.4%*	38.9%**
Group II (n=21)	23.8%	9.5%**
Group III (n=38)	15.8%*	5.2%**

* p I-III - < 0.05; ** p I-II and p I-III - <0.01

Table 2. The incidence of auto-Abs overproduction for all measurements and their mean values in children of different age groups.

Children groups	Abs overproduction	Mean values in groups M_n±m
Gr. I $n_I = 72$	26.4%**	29.0±4.2
Gr. II $n_{II} = 84$	8.3 %**	11.9±6.1
Gr. III $n_{III} = 152$	6.6%**	31.4±7.2

$n_{I,II,III}$ – the number of all measurements of auto-Abs performed in each group

pared to children aged 7 10 years (group II – 23.8%) and 11-16 years (group III – 15.8%) (Table 1).

The comparative analysis of increased auto-Abs levels in relation to all performed measurements in different age groups revealed the significant difference in cardiospecific autoantibodies overproduction in children of early and middle age groups (Table 2). The combined overproduction of auto-Abs was also statistically significant in children of early age, i.e. the increased levels of auto-Abs to two or more myocardial antigens (Table 1).

In the structure of auto-Abs overproduction (Fig. 1), the increased level of auto- Abs to COS-05 and β1AR in children of preschool age ($p<0.05$) was observed significantly more often. No increase in auto-Abs to COS-05 was observed in children older than 10 years.

Decreased serum level of cardiospecific autoantibodies in children with HRCD ranged from 50% in group I to 71.7% in group III.

DISCUSSION

The analysis of integrated immunochemical data showed that normal serum levels of all investigated cardiospecific autoantibodies was observed only in 5.2% of investigated children with HRCD. The abnormally decreased levels of the majority of investigated autoantibodies was observed in 2/3 of children. No specificity was revealed in production of different auto-Abs.

The increased production of some cardiospecific auto-Abs was revealed in 1/4 of patients with HRCD. The increased levels of auto-Abs to cytoplasmatic myocardial proteins COS-05 and β1-adrenoreceptors predominated.

The overproduction of auto-Abs was 2-3-fold higher in preschoolers. The overproduction of auto-Abs to membrane/cytoskeleton antigen was revealed only in children below 11 years of age.

The most frequent increase in autoantibodies to soluble cytoplasmatic antigen predominantly responsible for development of functional and metabolic changes in the myocardium (i.e. for impaired energetic and plastic processes in myocardiocytes) suggests a prevalence of functional and regulatory dysfunction rather than organic myocardial damage in children with arrhythmias.

However, in some children (mostly in preschoolers) with overproduction of auto-Abs to membrane/cytoskeleton antigen of the myocardium (CoM-05), the induction of destructive changes in myocardium may be potentially supposed due to complement-dependent lysis and/or antibody-dependent cellular cytotoxicity (6).

The increased levels of auto-Abs to β1–adrenoreceptors may, on one hand, lead to impaired functioning of these receptors, gradual changes of their density and development of myocardium remodeling with the left ventricular dysfunction. One the other hand, the increased production of such auto-Abs may be the secondary reaction and reflect the primary abnormal increase in membrane expression/destruction of respective receptors, casually related to metabolic disorders or to effects of infectious agents.

The increased levels of auto-Abs to membrane antigen of myocardiocytes and β1-adrenoreceptors revealed in a small proportion children with HRCD, may be suggestive of primary or secondary immune-mediated inflammatory changes in the myocardium in such patients, despite the absence of the evident clinical and instrumental data.

More marked overproduction of cardiospecific auto-Abs in children of early and preschool age and its commonly polyspecific nature (to several antigens), including Abs to cytoskeleton proteins, suggests that autoimmune nature of HRCD is more often revealed in younger children. This may be due to more frequent coincidence of arrhythmia manifestation and its diagnosis in this age group compared to others. In other words, the overproduction of cardiospecific auto-Abs possibly suggests the recent development of pathological process in the myocardium.

The abnormally low serum levels of cardiospecific autoantibodies revealed in 2/3 of investigated children indicate that, generally, in children with arrhythmias the most typical abnormality is the impaired elimination of natural catabolic products rather than immune-inflammatory (destructive) changes. It is obvious that excessive accumulation of such toxic and/or extra reactive products may lead to impaired functional activity of the myocardium.

Such conclusions may be considered as preliminary and requiring further clinical and experimental argumentation and investigation. These data are not yet sufficient to answer the main question – whether the observed immunological changes are primary (causing the typical changes in myocardial function) or secondary to primary changes in the myocardium due to other reasons. In any case, the obtained results force us to determine if it is reason-

able to use immunocorrective therapy in children with heart rhythm and conduction disturbances, and support the indication for anti-inflammatory therapy in patients with increased levels of auto-Abs to membrane/cytoskeleton antigen of myocardiocytes and β1-adrenoreceptors.

In the first approximation it may be quite reasonable to use therapy with parenteral normal immunoglobulins.

CONCLUSIONS

1. In children with heart rhythm and conduction disturbances, the multidirectional abnormalities in production/serum levels of cardiospecific autoantibodies were revealed which indirectly confirm the etiological and pathogenic heterogeneity of arrhythmias.
2. Generally, without considering the age,in children with arrhythmias the most typical abnormality is impaired elimination of natural catabolic products and impaired energetic and plastic processes in myocardiocytes rather than immune-inflammatory destructive changes in myocardium.
3. Polyspecific overproduction of anti-cardiac autoantibodies, which is most common in children with arrhythmias of early and preschool age, may suggest a recently developed immune inflammatory process in epy myocardium and supportы the indication for anti-inflammatory therapy.

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INFORMATION STATEMENT

Russian Cardiologists at PCR 2010

The conference PCR 2010 – the biggest International forum dedicated to the problems of percutaneous therapy and diagnostics was held in Paris on May 25-28, 2010. Paris Course of Revasculrization totally matches up to the slogan put on its cover – The Leading Cardiovascular Course. Over 13 thousands of specialists participated in this forum, and about 300 sessions, seminars and symposia on the most thrilling questions of our specialty have been held during the four days of its work. We shall give a more detailed account on the work of PCR 2010 in our next issue, and now we would like to mention the events of utmost significance for Russian cardiology that took place within the frames of this forum.

Obviously, the brightest of these events was the live transmission from Moscow City Center of Interventional Cardioangiology to the Main Arena of the Paris Palace of Congresses. During the plenary session "Percutaneous coronary intervention for complex ST-segment elevation myocardial infarction patients", three emergency endovascular procedures in patients admitted to the Center with the diagnosis "acute myocardial infarction" within the first hours after the onset have been performed in a live television broadcast.

Two sessions have been held under the auspices of the Russian Society of Interventional Cardioangiology: together with the Latvian Society of Interventional Cardiology – "Percutaneous coronary intervention in multivessel disease as an alternative to surgery" (Chairpersons D. G. Iosseliani and A. Erglis) - and together with the German Society of Angioplasty/Society of Vascular Medicine – "Endovascular therapy is a must and first line treatment in patients with critical limb ischemia" (Chairpersons Z.A. Kavteladze and K.L. Schulte). One more session – "After a failed percutaneous coronary intervention of coronary chronic total occlusion: what to do, when and how?" – has been held under the auspices of the Bulgarian and Siberian Working Groups for Interventional Cardiology (Chairpersons A. Doganov and A.G. Osiev)

Besides, D.G. Iosseliani was a panellist at the plenary session «Multivessel disease: patient stratification and treatment strategies», A.G. Osiev co-chaired the symposium "Drug-eluting stent in daily practice: rationale for selection", was a panellist at the plenary session "Percutaneous coronary intervention for complex ST-segment elevation myocardial infarction patients", and made presentations during several sessions and forums, while B.G. Alekyan was a facilitator at the seminar "Learning the techniques on complex multivessel disease with Jean Fajadet".