PROBLEMS OF RESTENOSIS IN THE CORONARY ARTERIES AFTER PERCUTANEOUS CORONARY INTERVENTIONS DURING IMPLANTATION OF METAL OR DRUG-COATED STENTS, DEPENDING ON CLINICAL DATA AND RISK FACTORS

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Article history:		Abstract:
Received:	April 11th 2023	To determine the difference between two types of stents: without and with a drug coating in the development of restenosis in the late stages after percutaneous coronary interventions (PCI), based on the initial clinical data and cardiovascular risk factors. The analysis included 32 patients with coronary artery disease: with holometallic stents (baremetal-stents – BMS) (n=15) and drug-coated stents (drug–elutingstents - DES) (n=17), subject to repeated coronary angiography performed according to clinical indications. All patients received appropriate antiplatelet and hypolipidemic therapy. During the index-PCI period, the group of DES patients, compared with the BMS group, was characterized by a significantly higher frequency of initial adverse signs, such as diabetes mellitus, smoker status, ACS. During the follow-up period, CAH in the DES group was less frequent than in the BMS group: restenoses were detected, repeated PCI was performed. The dynamics in risk factors during the follow-up period differed little between the groups.With follow-up periods extended to 2 years, taking into account the initial clinical data and SSR indicators, the effectiveness and validity of the use of drug-coated stents in comparison with uncoated stents is confirmed.
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INTRODUCTION. Today, percutaneous coronary interventions (PCI) occupy a leading position among invasive methods of treatment of coronary artery disease (CHD). Despite the constant development of PCI technology, the frequency of restenosis in the coronary artery stenting zone remains at a fairly high level and is about 15-57%. At the same time, the substrate of occlusion, as a rule, is not atherosclerosis, but fibrosis, which causes the complexity of repeated recanalization and a lower percentage of technical success in restoring blood flow. Timely diagnosis for the purpose of early detection of restenosis and its correction is an extremely urgent problem for practical healthcare, which causes scientific and practical interest in this issue and serves as the basis for this study.With all the evidence of better results when performing PCI with stents coated with antiproliferative agents than uncovered for short periods of observation, this conclusion becomes debatable for long periods [7]. The relationship of clinical data, cardiovascular risk factors and the type of stents used in the formation of the restenotic process for extended periods after PCI is considered in this publication.

MATERIAL AND METHODS: The study included 32 patients with repeated coronary angiography observations (CAG) up to 2.3 years after PCI with coronary artery stenting. The median mean follow-up period was 82.9 days. Indications for repeated intervention (CAG) were the appearance or increase of angina attacks or the development of acute coronary syndrome (ACS). In order to exclude patients with planned repeated interventions from the study, cases were not considered for a period of less than 30 days. Obtaining informed consent for the study was mandatory. The first study (index-PCI) included all the necessary clinical, biochemical studies, including non-invasive instrumental diagnostics and CAG. On the basis of the conducted examination, a decision was made and PCI balloon coronary angioplasty was performed according to the standard technique using stents without or with a drug coating. Further treatment recommendations included optimal drug therapy with dual antiplatelet therapy in accordance with the recommendations of the Russian Society of

Cardiology and statin therapy. Upon re-hospitalization, a similar examination was carried out with the decision to perform a coronary angiography. The coronary picture was assessed visually by two specialists and a narrowing of more than 20% of the lumen of the stented part of the artery was taken as restenosis. During the follow-up period, angioplasty of narrowing in the wall or in non-stented areas of the coronary artery was performed, if necessary, in order to eliminate incomplete myocardial revascularization. When analyzing the material under consideration, patients were divided into two groups, in which either holometallic stents (baremetal-stents - BMS) (15 patients) or drug–coated (drug-elutingstents – DES) from the limus group were used during the index-PCI period: sirolimus, everolimus, zotarolimus, biolimus (17 patients). Patients with a combination of stents were not included in the analysis.

The characteristics of the material under consideration (index-PCI and follow-up CAG) were based on taking into account the following clinical signs and the presence of the SSR factor: age, gender, type of implantable stent, the presence of restenosis; stable angina, postinfarction cardiosclerosis (PIC), ACS: acute myocardial infarction (AMI), unstable angina (NS); chronic renal insufficiency (CRF); hypertension, hypercholesterolemia, diabetes mellitus and insulin dependence, smoker status and smoking history, physical inactivity, obesity, alcohol abuse, burdened family history of CVD, weight, body mass index (BMI). Characteristics of clinical signs and factors of SSR in groups with different stents: At the time of inclusion in the study (index-PCI), the groups were comparable in many of the considered signs, including age, gender and such factors of SSR as dyslipidemia, obesity, insulin dependence in diabetes mellitus, alcohol abuse, smoking history, physical inactivity, burdened history of CVD, abdominal obesity, BMI, weight.There was a predominance in the use of DES in patients with unstable angina. There was no difference in myocardial infarction between the groups. Previously performed stenting with the formation of restenosis was more common in the DES group (Table 1).

Table 1
Characteristics of patients at the time of "index-PCI" with division depending on the type of implanted stent

Characteristics at the time of index PCI	SUM (n=32)	BMS (n=15)	DES (n=17)	R
Age	60,55±8,62	60,51±8,46	60,61±8,88	0.944
Male gender	74,47	75,32 %	73,44 %	0.798
The presence of restenosis*	4,96 %	1,30 %	9,38 %	0.047
Hypertension	87,94 %	93,51 %	81,25 %	0.037
Dyslipidemia	41,84 %	42,86 %	40,63 %	0.789
Fatness	32,62 %	33,77 %	31,25 %	0.751
Diabetes mellitus	19,15 %	10,39 %	29,69 %	0.004
Insulin dependence	4,26 %	3,90 %	4,69 %	1.000
Stable angina pectoris	79,43 %	87,01 %	70,31 %	0.015
OKS	20,57 %	12,99 %	29,69 %	0.015
OIM	10,64 %	7,79 %	14,06 %	0.229
NS	9,93 %	5,19 %	15,63 %	0.049
Alcohol abuse	15,60 %	12,99 %	18,75 %	0.348
Family history of CVD	43,26 %	44,16 %	42,19 %	0.814
Physical inactivity	14,18 %	12,99 %	15,63 %	0.655
Abdominal obesity	9,22 %	9,09 %	9,38 %	0.954

*AMI – acute myocardial infarction, ACS – acute coronary syndrome, NS – unstable angina, CVD – cardiovascular diseases, PCI - percutaneous coronary intervention, BMS – bare–metalstents (holometallic stents), DES– drug-elutingstents (drug-coated stents). The p value corresponds to the comparison of the BMS and DES groups. * – restenoses in the previous PCI.*

At the time of repeated (follow-up observation of CAH), the groups were comparable in the following indicators – age, dyslipidemia, insulin dependence in diabetes mellitus, stable angina pectoris, PEAKS, ACS, unstable angina pectoris, the difference was in the following indicators – time before follow-up, repeated PCI, hypertension, diabetes mellitus.In the interval between the stages of index-PCI and follow-up CAH, myocardial infarction was suffered by 9 patients with BMS 11.69% and 5 patients with DES 7.81% (p=0.5), and, in addition, with follow-up CAH, it was the cause of the study in 6.49% of patients with BMS and 4.69% of patients with DES(p=0.728), and all patients were re-stented; unstable angina was present in 9.09% of

patients with BMS and in 6.25% of patients with DES (p=0.7).In general, in the material under consideration, restenoses were detected in 27% of patients among 32 patients.In patients with BMS – restenosis was detected in 35.06%, and all patients underwent PCI. Among patients with DES, restenoses were detected in 18.75% of patients during repeated angiographic examination, and 66.8% of them underwent repeated PCI. In patients without restenosis in the stent with follow-up CAH, the basis for performing PCI was angiographic indications of an increase in the degree of narrowing in non-stented areas of the coronary arteries, or incomplete myocardial revascularization was eliminated

Table 2
Characteristics of patients at the time of follow-up (follow-up CAG) with division depending on the type of implanted stent

Characteristics at the time of the Follow-Up	Sum(n=32)	BMS (n=15)	DES (n=17)	R
The presence of restenosis	15	11	4	0.031
Performing PCI	71,63 %	80,52 %	60,94 %	0.010
Dyslipidemia	52,48 %	54,55 %	50,00 %	0.591
Stable angina pectoris	86,52 %	84,42 %	89,06 %	0.421
OKS	13,48 %	15,58 %	10,94 %	0.421
AMI after stent implantation with index-PCI Characteristics at the time of the Follow-Up The presence of restenosis Performing PCI	5,67 %	6,49 %	4,69 %	0.728

MI – myocardial infarction, CAG – coronary angiography, NS – unstable angina, ACS – acute coronary syndrome, PCI – percutaneous coronary intervention, BMS – bare-metalstents (holometallic stents), DES– drug-elutingstents (drug-coated stents).

DISCUSSION: Among patients with PCI performed with the use of drug–coated and non-drug-coated stents, the deterioration, during 2 years of follow-up, may be associated with both the natural course of coronary heart disease - alternating periods of stabilization and an increase in symptoms due to violations in drug therapy or changes in functional load and lifestyle, – The same is true with morphological factors: progression of coronary atherosclerosis or restenosis in the stented part of the CA [10].An important question remains: does the effect of two types of stents on the course of coronary disease in

the long term differ: with and without a drug coating – because, despite all the obvious advantages of drug-coated stents, a number of recent observations do not provide unambiguous confirmation of the benefits of drug coating [3]. In the works on the analysis of long-term results of stenting of drug-coated stents, several poorly understood causes of developing complications are identified: and, first of all, acute and subacute delayed thrombosis caused by the phenomenon of neoatherosclerosis of the vascular wall in the stenting zone, and in some cases with fatal outcomes [5].In our study, in 28% on average, the deterioration of the

clinical condition coincided with changes in the stented segment of the coronary artery or in the immediate vicinity of the stent, at the same time, in patients with drug-coated stents, deterioration was less frequent (19%) than when using holometallic stents (35%). It is important to emphasize that these figures follow from the analysis of a selected group of patients with repeated clinical manifestations and are very similar to a study comparing different types of stents, where follow-up is designated as the endpoint 6-8 months after stenting: without taking into account clinical necessity, angiographic restenosis was detected on average in 26.4% of patients, while with DES in 12.2-14.6% and with BMS in 30.1% [5]. Some differences in the clinical baseline characteristics of the groups in our study are associated with an obvious preference for DES in previously stented patients with diabetes mellitus and unstable angina, but it is known that these factors generally negatively affect the outcome and in our study enhance the positive significance of drug-coated stents.According to intracoronary imaging, several causes leading to the development of restenoses are identified: neointimal hyperplasia and technological failures of stenting. These problems were common to all types of stents, but differed in frequency: with BMS, NG prevails, and with DES, stent under–opening and destruction.The problem of late restenosis in stents in the long term after the intervention can be considered as the formation of a new variant of vasculopathy after PCI, which differs in morphological features from proliferative smooth muscle narrowing in the early time stages after stenting. These are elements peculiar to atherosclerosis, which allowed us to formulate the term – neoatherosclerosis. Predominant development of neoatherosclerosis in drug-coated stents in the long term after PCI, confirmed by intracoronary imaging and clinical picture of acute thrombosis.

CONCLUSIONS: To date, many scientific papers have been published aimed at studying the problem of coronary artery restenosis. However, in general, the problem of coronary artery restenosis remains unresolved, most of the work in this direction is devoted to the choice of the method of revascularization, and not to the prevention of restenosis, there is no clear "hierarchy" of risk factors for the development of restenosis after endovascular stenting. With long-term follow-up, taking into account the initial clinical data and SSR indicators, the effectiveness and validity of the use of drug-coated stents in comparison with uncoated stents is confirmed.

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