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Various Clinical And Angiographic Characteristics Of Patients With Coronary Heart Disease And Their Impact On The Development Of Early And Late Restenosis

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Abstract.

Objective: To evaluate the clinical and angiographic characteristics of patients depending on the period of development of restenosis.

Material and methods: The study included patients who underwent implantation of drug-eluting stents of both the first and second generation. All patients who underwent implantation of the stent without complications (in the first 10 days) were offered a repeated phased clinical examination. Of this observation group, in 62 patients with repeated coronary angiography (CAG), restenosis within the stent was detected more than 50% of the proper lumen of the vessel. The observation period for patients ranged from 3 months. up to 4 years (median follow-up = 2.53 ± 1.29 years). The number of patients for whom PCI was performed ≤ 1 year ago (on average 0.93 ± 0.22) was 22 (35.5%) patients - A-subgroup. The number of people who had PCI performed> 1 year ago (on average 3.30 ± 0.85) was 40 (64.5%) people - the B-subgroup.

Results: The first year after PCI is a critical period in terms of the risk of developing restenosis for women, for people with severe obesity (average BMI = 33.42 ± 6.29 kg / m2), the presence of diabetes mellitus and a large long vascular lesion (average length = 32.25 ± 12.21 mm). According to the results of our study, angiographic adverse predictors of the development of restenosis turned out to be a large length of atherosclerotic plaque (average plaque length = 28.88 ± 9.79 mm), small diameter of the target artery (average values = 3.16 ± 0.46 mm), at the same time, the risk of developing restenosis in the first year of observation was associated with the presence of multivascular lesions and the performance of several simultaneous recanalizations.

The role of the SYNTAX and TIMI rating scales, established in the earlier large-scale clinical trials, has proved its effectiveness in assessing the risk of developing restenosis in the first year of observation. Namely, a high average SYNTAX score (average values - 14.06 ± 2.38) and a low average TIMI score (average values - 0.69 ± 0.70) were associated with early (in the first 12 months after PCI) development "In-stent" restenosis.

Conclusion: The study demonstrates the need for further in-depth study of the problem of restenosis in order to identify not only new, but also easily accessible clinical predictors of their development, which will subsequently allow the development of preventive measures.

Keywords: restenosis, first year of observation, PCI, clinical and angiographic predictors

Relevance.

For many years, circulatory system diseases have been leading in the death rate of the planet's population. Recent WHO data suggest that cardiovascular disease (CVD) causes more than 30% of all deaths in the world every year. In 2005, 17 million deaths were caused by pathology of the cardiovascular system, of which 7 million were due to ischemic (coronary) heart disease (CHD) and more than 5.5 million were caused by pathology of the cerebrovascular system [1].

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At the present stage, the most significant results of the treatment of atherosclerotic vascular lesions are shown by endovascular technologies, in particular coronary angioplasty by vascular stenting. The share of the stenting procedure from all therapeutic interventions on the vessels of the heart is on average 70% [2].

The introduction of the stenting procedure into practice significantly improved the results of endovascular treatment of coronary artery disease in comparison with balloon angioplasty. So, the frequency of development of restenosis of the coronary artery decreased by an average of 50% and is currently 10–40% according to various authors [3].

Restenosis is the most common complication of stenting and angioplasty, which can occur both during the first days after the procedure and after several months or even years. An angiographic definition of restenosis is a repeated narrowing of the coronary artery at the site of stent placement, leading to a decrease in the diameter of its lumen by more than 50%, which occurs during the repair of the arterial wall after its damage. [4,5]. Nevertheless, the data regarding the predictors of development and the time of formation of restenosis are ambiguous and controversial, and therefore the aim of our study was: to evaluate the clinical and angiographic characteristics of patients depending on the period of development of restenosis.

Material and methods.

From 2015 to 2019, patients with coronary artery disease who underwent stenting were observed clinically for five years after invasive intervention. The study included patients who underwent implantation of drug-eluting stents of both the first and second generation. All patients who underwent implantation of the stent without complications (in the first 10 days) were offered a repeated phased clinical examination. From this observation group, in 62 patients, repeated coronary angiography (CAG) revealed restenosis inside the stent, with a volume of more than 50% of the proper vessel lumen. The observation period for patients ranged from 3 months. up to 4 years (median follow-up = 2.53 ± 1.29 years). The number of patients who ≤ 1 year ago (on average 0.93 ± 0.22) underwent PCI was 22 (35.5%) patients — the A-subgroup. The number of people who had PCI performed> 1 year ago (on average 3.30 ± 0.85) was 40 (64.5%) people - the B-subgroup.

The criteria for inclusion in this study were:

- Patients with a diagnosis of coronary heart disease, established by the results of clinical and instrumental examination.
- Patients with documented painless ischemia, stable and unstable angina pectoris, acute myocardial infarction and history of myocardial infarction.
- Signed informed consent of the patients themselves or their close relatives.

The exclusion criteria were:

- Patients with severe concomitant pathology of the cardiovascular system (aortic aneurysm; valvular pathology requiring surgical correction; severe left ventricular systolic dysfunction (LVEF <35%); decompensated heart failure).
- Patients not tolerant of anticoagulants / antiplatelet agents.
- Persons with bifurcation lesions, stem lesions of the coronary bed.
- Patients with medium and high risk of PCI in the SYNTAX scale.

All patients included in the study underwent general clinical and laboratory examinations (general blood test, biochemical blood test, coagulogram, ECG in 12 standard leads, echocardiography with myocardial contractile function assessment, if necessary - daily ECG

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monitoring), as well as coronary angiography (CAG) with assessment size, location and form of restenosis. To assess the latter, was used R. Mehran classification.

Statistical analysis

Statistical processing of the results was carried out on a Pentium-IV personal computer using the STATISTICA 6 software package. Calculate the arithmetic mean (M) and root-mean-square (standard) deviation (SD).

In our study to avoid statistical inaccuracy, the analysis was accompanied by a check on the normal distribution of clinical signs.

To compare the arithmetic means of the two groups, the t-student test was used. To assess the presence of relationships between indicators, a correlation analysis was performed with the calculation of the Pearson correlation coefficient. To analyze the reliability of differences between qualitative signs, the $\chi 2$ criterion was used.

Ethical aspects.

The study was conducted in accordance with the principles of the Helsinki Declaration.

The results of the study.

The study revealed that patients in the A-subgroup were 1.4 years younger, than patients in the B-subgroup (Table 1). The weight characteristics of patients in the A-subgroup turned out to be 5.67 kg more than in patients of the B-subgroup. This was reflected in the body mass index (BMI), which was 2.74 kg / m2 higher in patients of the A subgroup ($p < 0.05$). Despite the relatively small number of patients with overweight and obesity, however, in patients of the A-subgroup, the average degree of obesity was greater than in the B-subgroup. Also patients with A subgroups were dominated by individuals with type 2 diabetes mellitus (DM) ($p < 0.05$) and with hypertension (AH) (Table 1).

Table 1.

Clinical characteristics of patients depending on the length of the period of development of restenosis

Index	**A subgroup (≤ 1 year) n = 22**	**B-subgroup (> 1 year) n = 40**	**p**	**$\chi 2$**
Age, years	59,36±9,52	60,75±9,41	0,551	
Men, n (%)	18 (81,8%)	36 (90,0%)	0,154	2,035
Women, n (%)	4 (18,2%)	4 (10,0%)		
Weight, kg	96,00±17,39	90,33±12,73	0,147	
BMI, kg / m2	33,42±6,29	30,68±3,74	0,035	
Number of overweight patients, n (%)	4 (18,2%)	14 (35,0%)	0,929	0,008
The number of patients with obesity 1-3 degrees, n (%)	8 (36,4%)	22 (55,0%)	0,255	1,298
Medium grade of obesity	1,75±0,89	1,36±0,66	0,054#	
History of myocardial infarction (HMI), n (%)	14 (63,6%)	32 (80,0%)	0,269	1,222
PMI single, n (%)	12 (54,6%)	18 (45,0%)	0,650	0,206
PMI multiple, n (%)	2 (9,1%)	14 (35,0%)	0,054#	3,715
The presence of DM, n (%)	12 (54,6%)	10 (25,0%)	0,040	4,199
The presence of AH, n (%)	22 (100,0%)	38 (95,0%)	0,753	0,099

Notes: n - is the number of patients; BMI - body mass index; PMI - a previous myocardial infarction in history; DM - diabetes mellitus; AH - arterial hypertension; p - significance of differences between subgroups; # - a tendency towards significance of differences between subgroups.

In terms of gender, a comparative analysis revealed that in the A-subgroup the number of women was greater than in the B-subgroup: 18.2% vs 10.0% (p> 0.05), i.e. in women, in the first year after PCI with stenting, the risk of developing restenosis was higher (Table 1). From this it follows that the first year of observation after stenting of the coronary arteries is critical for females in terms of the risk of developing restenosis.

A separate analysis of data on a previous myocardial infarction (PMI) in history also revealed a number of interesting facts. Namely, in the A-subgroup the number of patients with PMI in the anamnesis was 16.4% less than in the B-subgroup. In this case, multiple PMI in the anamnesis prevailed in patients of the B-subgroup, amounting to 35.0% (p = 0.054), and in patients of the A-subgroup, on the contrary, a single transferred PMI prevailed - 54.6% (Table 1).

Table 2.

Angiographic characteristics of patients depending on the duration of the period of development of restenosis

Index	**A subgroup (≤ 1 year) n = 22**	**B-subgroup (> 1 year) n = 40**	**p**	**χ2**
LAD, n (%)	14 (63,6%)	34 (85,0%)	0,007	10,528
LCX, n (%)	8 (36,4%)	12 (30,0%)	0,452	0,565
OM, n (%)	2 (9,1%)	2 (5,0%)	0,406	0,691
RCA, n (%)	8 (36,4%)	22 (55,0%)	0,011	6,533
PIA, n (%)	6 (27,3%)	2 (5,0%)	0,000	16,406
Σ CA	1,73±1,08	1,80±0,76	0,767	
L, mm	32,25±12,21	27,69±18,49	0,304	

Notes: n - is the number of patients; LAD - Left anterior descending artery; LCX - Left circumflex coronary artery; OM - Obtuse marginal branch; RCA - Right coronary artery; PIA - Posterior interventricular artery; *Σ CA – average number of affected coronary arteries per 1 patient; L - the average total length of all vascular lesions per 1 patient; p - significance of differences between subgroups at p <0.05.*

According to coronary angiography, it was found (Table 2) that in patients of the A-subgroup, the basins of the envelope of the LCX (p> 0.05), OM (p> 0.05) and PIA (p <0.05) arteries were the most vulnerable. , while in patients of the B-subgroup, the basins of PMA and PKA were more often involved in the pathological process (both p <0.05).

The calculation of Σ CA (average number of affected coronary arteries) per 1 patient in the A-subgroup was 1.73 and in the B-subgroup - 1.80 per 1 patient (p> 0.05). Nevertheless, the average total length (L, mm) in patients of the A-subgroup turned out to be 32.2 ± 12.6 mm and in the B-subgroup 27.7 ± 18.9 mm (p> 0.05).

To identify angiographic predictors of coronary artery restenosis, we analyzed previous recanalization procedures among patients of group 2. The following factors were taken into account: the average length of the atherosclerotic plaque (L ASP, mm); the average diameter of the artery (d, mm) and, in the case of multivascular lesions, the number of simultaneous recanalizations. Unfortunately, it was not possible to evaluate the stiffness of ASB and the degree of malapposition (full disclosure) of the stent in our study, due to the lack of optical coherence tomography (OCT) and intravascular ultrasound (IVUS).

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From these positions, it was found that in patients of the A-subgroup, initial recanalization was carried out on vessels of smaller diameter and with longer lesions (both p> 0.05). The latter, in turn, required the implantation of a larger number of stents (Table 3).

The number of patients with multivascular lesions in the A-subgroup was less than in the B-subgroup, however, simultaneous recanalizations among the respondents of the A-subgroup prevailed by 4.2% (Table 3).

Table 3.

Primary angiographic characteristics of patients with restenosis

Index	**A subgroup (≤ 1 year) n = 22**	**B-subgroup (> 1 year) n = 40**	**p**	**χ2**
L ASP, mm	28,88±9,79	25,60±8,06	0,161	
Number of Stents Installed	30	51		
Number of stents per 1 patient	1,36	1,27		
d, mm	3,16±0,46	3,34±0,51	0,174	
Number of patients with multivascular lesions, n (%)	12 (54,5%)	24 (60,0%)	0,882	0,022
Number of simultaneous recanalizations, n (%)	3 (25,0% от 12 б/х)	5 (20,8% от 24 б/х)	0,887	0,020
SYNTAX score	14,06±2,38	10,89±3,31	0,000	
TIMI score	0,69±0,70	1,07±0,69	0,043	

Notes: L ASP - the length of the atherosclerotic plaque; d - the diameter of the artery; n – number of patients.

Assessment of the CAG data on the SYNTAX scale showed a relatively high score among the respondents of the A-subgroup (p <0.0001), which indicated a higher level of risk of complications during the PCI procedure. Nevertheless, the average score in both the A-subgroup and the B-subgroup was ≤ 22 points, which, according to American colleagues, confirms the correctness of PCI in these patients [6].

Assessment of coronary blood flow according to the TIMI scale found that the average score was ≈ 1.5 times lower in respondents of the A-subgroup than in patients of the B-subgroup (p <0.05). At the same time, the number of patients for whom there was a lack of antegrade blood flow during contrasting (TIMI = 0), in the A subgroup amounted to 10 (45.4%) and in the B subgroup 8 (20.0%) people (p = 0.069 and $\chi 2 = 3.314$).

Also, according to the analysis of previous recanalization procedures, it was found that 1 patient (1.6% of the total number of patients with restenosis) developed acute stent thrombosis on the first day after PCI and 1 respondent (1.6%) had edge stent dissection, which required a second intervention and the installation of an additional stent. Both of these cases were noted in patients of the A-subgroup, in whom restnosis developed during the first year of observation.

Discussion.

Over the long period of performing percutaneous coronary intervention (PCI), as one of the modern methods of treating coronary heart disease (CHD), sufficient experience has been gained in understanding the positive and problematic issues of the course of coronary disease after the procedure. Neointimal hyperplasia and fibromuscular proliferation, which developed in

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response to an established metal frame in the coronary arteries, was reduced by stents with a drug antiproliferative coating [7]. As the follow-up time increased, a new wave of serious clinical complications associated with a change in previously stented coronary arteries was noted. A new process found in a stented coronary artery was similar to native atherosclerosis and is described in the literature as neoatherosclerosis [8,9].

Based on our study and analysis of clinical and angiographic parameters, the most significant predictors of the development of coronary artery restenosis depending on the period of its development were identified. They turned out to be: sex, obesity, diabetes mellitus - on the one hand, and a large length of ASP, a small diameter of the artery, a large number of simultaneous recanalizations in multivascular lesions, a relatively high risk on the SYNTAX scale and a low score on the TIMI scale - on the other hand. All these indicators are available during routine examination of the patient. At the same time, according to some scientists [10], there is a risk of complications after revascularization between the female sex, obesity, and a violation of carbohydrate metabolism. On the contrary, according to other researchers, risk factors for the development of atherosclerosis, such as age, gender, hypertension, hypercholesterolemia, diabetes mellitus, insulin dependence, smoking, alcohol abuse, burdened family history of CVD, hypodynamia, abdominal obesity, BMI, have not reached significant significance with late restenosis. Hypodynamia and abdominal obesity had a paradoxical negative value in groups of patients with restenosis [9].

Stenting of small-diameter arteries and the number of implanted stents are well-known predictors of restenosis when using drug-eluting stents [11,12], which was also the case in our study and was confirmed by the corresponding scores on the SYNTAX and TIMI scales.

However, our study is retrospective, with repeated coronary angiography performed only in patients hospitalized with a worsening clinical condition.

Conducted in world practice, scientific research reveals more and more new indicators and predictors of the development of restenosis of coronary arteries, not only clinical or angiographic, but also laboratory and even genetic in nature. In particular, a number of authors [13] have developed a scale for assessing the risk of developing restenosis in drug-eluting stents. The markers we have identified are consistent with data from other researchers and are available in the everyday clinical practice of cardiologists and angiosurgeons.

Conclusions:

1. The development of restenosis within 1 year after PCI is more often associated with the female sex, the presence of a more pronounced degree of obesity, diabetes mellitus and a longer vascular lesions.
2. According to coronary angiography, the development of restenosis within 1 year after PCI is characterized by lesions of the arterial basins of the LAD, LCX, OM, RCA and PIA, while the lesions of the LAD are prevailing (accounting for 63.6% of cases).
3. The angiographic predictors of the development of restenosis during the first year of observation were the long length of the ASB, the small diameter of the artery, the greater the number of simultaneous recanalizations in multivascular lesions, the relatively high risk on the SYNTAX scale and the low score on the TIMI scale.

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