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Acute coronary syndrome — a frequent clinical manifestation of bare metal in-stent restenosis

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Abstract

Background: In-stent restenosis (ISR) complicates 20–30% of percutaneous coronary interventions (PCI) with bare metal stent (BMS) implantation. Although the widespread use of drug eluting stents (DES) across Europe caused a considerable reduction of BMS implantations, their number is still lower than the number of BMS implantations in several countries.

Aim: The clinical presentation of ISR has not been well characterissed. Thus, we attempted to analyze this condition and assess the treatment of ISR in everyday clinical practice.

Methods: We searched our database for all cases of bare metal ISR between 1999 and 2007. Follow-up angiography after PCI was not a routine procedure but a clinically driven examination. Clinical presentations of ISR were divided into: stable angina, and acute coronary syndromes (ACS), i.e. unstable angina (UA) and myocardial infarction (MI) (further subdivided into NSTEMI and STEMI). Analysis included variables associated with different clinical manifestations, methods of ISR treatment and in-hospital complications of ISR.

Results: In-stent restenosis was identified in 432 (3%) of 15,910 patients who underwent PCI. The mean age was 61.6 ± 15.6 (27–86) years, and 295 (68.3%) patients were men. Risk factor distribution was typical for a Caucasian population. Recurrent clinical episode occurred at a mean of 7 (1–108) months after PCI. Exertional angina was present in 245 (56.7%) patients, UA in 128 (29.6%) patients and MI in 59 (13.7%) patients, including STEMI in 28 (6.5%) and NSTEMI in 31 (7.2%) patients. Overall, ACS was diagnosed in 187 patients or 43.3% of all cases of ISR. Multivariate analysis showed a positive correlation between previous MI and younger age and ACS as the clinical manifestation of ISR, and a negative correlation between more severe restenosis and ACS manifestation. The incidence of clinical complications (MI or death) was higher in patients with ACS as the clinical manifestation of ISR (6.9% *vs* 1.6%).

Conclusions: In-stent restenosis after BMS implantation is a serious clinical problem. More than 40% of patients with ISR present with ACS, including 13.7% patients with MI, more frequently among younger patients and patients with previous MI. Most patients with ISR are treated with repeated PCI with high success rate (97.7%), although the risk of clinical complications is considerably higher in patients presenting with ACS.

Key words: in-stent restenosis, bare metal stent, acute coronary syndrome

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INTRODUCTION

The number of percutaneous coronary interventions (PCI) is growing worldwide. In most cases, PCI includes stent implantation. Despite improved technique and advances in stent design, bare metal stent (BMS) implantation continues to be associated with a significant risk of in-stent restenosis (ISR), considered the Achilles heel of interventional cardiology. Estimated rate of ISR ranges from 15% to 60% [1–5]. The occurrence of restenosis following BMS implantation is related to stent design, implantation technique and, most importantly, patient-related factors. These include demographic factors such as age, diabetes, renal failure, and angiographic factors, such as vessel reference diameter, minimal lumen diameter, an d stent length [1–4, 6, 7]. A major advance in comba-

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ting ISR has been the introduction of drug eluting stents (DES) that largely superseded BMS in many countries. Initial enthusiasm for DES implantation lessened, however, with reports of late and very late stent thrombosis being more frequent in DES recipients compared to BMS recipients [8, 9]. In addition, a number of randomised studies and large prospective registries failed to show reduction of mortality and recurrent infarction rate with DES implantation [9–11]. Bare metal stents remain the most commonly used stents in Poland, mainly for economic reasons. With continuously growing number of PCI procedures, the number of patients presenting with symptoms of ISR is also rising. In-stent restenosis is usually perceived as a benign condition, and its treatment seemed to be associated with a low rate of complications. However, some recent reports questioned this view, resulting in revision of our approach to ISR.

The purpose of this study was to analyse clinical manifestations of ISR in patients treated in a single invasive cardiology centre.

METHODS

Study group

In 2000–2007, 8243 PCI procedures and 15,910 coronary angiographic studies were performed in our cardiac catheterisation lab. We search our database to identify patients who underwent a follow-up coronary angiography due to recurrent clinical symptoms and were found to have restenosis following PCI with BMS implantation. We identified 432 with a first episode of ISR. Recurrent ISR episodes in the same patient were excluded

In-stent restenosis

Angiographic restenosis was defined as recurrent stenosis of more than 50% of lumen diameter, identified in the stent or within 5 mm from its borders, and occurring at least one month after the primary intervention. In patients with multivessel disease, clinical symptoms were attributed to ISR and not lesions in other vessels based on operator experience and the presence of these lesions in the previous coronary angiography. One case of restenosis within a LIMA-LAD graft and one case of restenosis within a venous graft were not included in our analysis due to a low number of such cases.

Indications for follow-up coronary angiography were established individually by a physician based on overall clinical picture. Follow-up coronary angiography after PCI was not performed routinely. Analysis of the follow-up coronary angiogram included determination of the location and degree of recurrent stenosis using quantitative assessment (GE Innova 2000, GE Medical Systems Ltd). Angiographic type of restenosis was determined using Mehran classification [12].

Clinical manifestation of ISR

Clinical manifestations of ISR were divided into the following categories: stable angina pectoris (with further class subdivision according to the Canadian Cardiovascular Society — CCS) and acute coronary syndromes (ACS) that included unstable angina, ST segment elevation myocardial infarction (STEMI), and non-ST segment elevation myocardial infarction (NSTEMI). Due to recent changes in myocardial infarction (MI) definition, ACS diagnosis was based on hospital discharge documentation that included diagnosis based on the current guidelines.

Care following coronary angiography

Information on further clinical management was retrieved from hospital discharge documentation. If repeated coronary angioplasty was performed, its angiographic effectiveness was analyssed, defined as residual stenosis of less than 30%. Procedural complications were divided into angiographic, including acute occlusion, no-reflow, peripheral embolism, perforation and large collateral vessel occlusion, and general, including death, MI and need for another revascularisation procedure during the same hospitalisation.

Statistical analysis

Continuous variables are presented as mean values and standard deviations and compared using the Student *t* test or the Mann-Whitney U test. Categorical variables are presented as percentages and compared using χ^2 test or the Fisher test (in case of low numbers in particular groups). Multivariate regression analysis was performed to identify prognostic variables. The differences between groups were considered significant when p value was < 0.05. Statistical analysis was performed using Statistica 6.0 software (StatSoft).

RESULTS

The mean age of the patients was 62 years (range 27–61 years). Men comprised 68.3% of the study group, with similar proportion in subsets with ACS and stable angina. The prevalence of atherosclerosis risk factors (tobacco use, diabetes, hyperlipidaemia, hypertension) was similar in both groups, with renal failure more common, and positive family history of coronary artery disease less common among ACS patients. The ACS patients had more comorbidities, including more patients with previous MI or stroke or coexisting chronic pulmonary disease.

The ACS patients significantly more often underwent primary angioplasty due to ACS (57.2% *vs* 38.7%, $p = 0.0005$).

At the diagnosis of ISR, the same proportion of patients in both groups received acetylsalicylic acid, thienopyridines, beta-blockers and calcium channel blockers. In contrast, ACS patients were more often treated with statins and angiotensin-converting enzyme inhibitors.

Recurrent clinical symptoms leading to follow-up coronary angiography due to ACS occurred earlier compared to exacerbation of stable angina pectoris (6 *vs* 9 months). Symptoms of severe heart failure (NYHA class III/IV) were uncommon and occurred in 2.8% of patients with ACS and 3.3% of patients with stable angina (NS) (Table 1).

Lesions treated with primary angioplasty were similar, according to AHA/ACC criteria, in both groups. The rate of reca-

Table 1. Comparison of demographic and clinical characteristics of patients with acute coronary syndrome and stable angina

	Overall (n = 432)	Acute coronary syndrome (n = 187)	Stable angina pectoris (n = 245)	P
Age (median, min–max)	62.1 ± 10 (27–86)	63.2 (27–86)	61.1 (36–84)	0.03
Men	295 (68.3%)	125 (66.8%)	170 (69.4%)	0.57
Current smokers	37 (8.5%)	10 (5.4%)	27 (11.0%)	0.1
Former smokers	102 (23.6%)	44 (23.5%)	58 (23.7%)	0.1
Diabetes	102 (23.5%)	52 (27.8%)	50 (20.4%)	0.07
Hyperlipidaemia	199 (46.1%)	83 (44.4%)	116 (47.4%)	0.54
Hypertension	323 (74.8%)	142 (75.9%)	181 (73.9%)	0.63
Renal failure	41 (9.5%)	24 (12.8%)	17 (6.9%)	0.04
History of stroke/TIA	15 (3.5%)	11 (5.9%)	4 (1.6%)	0.03
Peripheral arterial disease	56 (13.0%)	28 (15.0%)	28 (11.4%)	0.28
Family history of coronary artery disease	100 (23.1%)	32 (17.1%)	68 (27.8)	0.009
Chronic lung disease	18 (4.2%)	14 (7.5%)	4 (1.6%)	0.006
Previous MI	230 (53.2%)	114 (61.0%)	116 (47.3%)	0.005
Previous CABG	21 (4.9%)	5 (2.7%)	16 (6.5%)	0.06
NYHA class				0.48
I	397 (91.8%)	173 (92.5%)	224 (91.4%)	
II	24 (5.6%)	10 (5.4%)	13 (5.3%)	
III	11 (2.6%)	3 (1.6%)	8 (3.3%)	
IV	1 (0.2%)	1 (0.5%)	0 (0%)	
Clinical status at the time of primary PCI				0.0005
Stable angina	230 (53.3%)	80 (42.8%)	150 (61.3%)	
Unstable angina	137 (31.7%)	70 (37.4%)	67 (27.3%)	
NSTEMI	52 (12%)	27 (14.5%)	25 (10.2%)	
STEMI	13 (3%)	10 (5.3%)	3 (1.2%)	
Medications				
Acetylsalicylic acid	419 (97%)	179 (95.7%)	240 (97.6%)	0.18
Thienopyridine	190 (44.0%)	73 (39.0%)	117 (47.5%)	0.07
Statin	317 (73.4%)	155 (82.9%)	162 (66.1%)	0.002
Angiotensin-converting enzyme inhibitor	345 (79.9%)	163 (87.2%)	182 (74.4%)	0.002
Beta-blocker	297 (68.8%)	133 (71.1%)	164 (66.9%)	0.45
Calcium channel blocker	65 (15.1%)	23 (12.3%)	42 (17.1%)	0.14
Time from primary PCI (months, median, min–max)	7 (1–108)	6 (1–108)	9 (2–92)	0.000008

TIA — transient ischaemic attack; MI — myocardial infarction; CABG — coronary artery bypass grafting; STEMI — ST elevation myocardial infarction; NSTEMI — non-ST elevation myocardial infarction; PCI — percutaneous coronary intervention

nalisation of chronic occlusion was significantly lower in patients presenting with symptoms of ACS. The number, length and diameter of implanted stents were similar in both groups.

The degree of coronary restenosis was similar in both groups. In patients with ACS, restenosis was more commonly noted in the left coronary artery branches than in the right coronary artery. No significant differences were seen in distribution of restenosis types according to the Mehran classification (Table 2).

Stable angina was the clinical manifestation of ISR in 56.7% of patients. Unstable angina was diagnosed in 29.6% of patients, and MI in 13.7% of patients, including NSTEMI in 7.2% and STEMI in 6.5% (Table 3).

Most patients with ISR (n = 340, 78.7%) underwent repeated PCI, including balloon angioplasty in 56.8% of cases, additional BMS implantation in 14.4% of cases, and DES implantation in 28.8% of cases. The data do not reflect the current practice of DES implantation in cases of ISR, as they include a period before introduction of DES. Patients with ACS had BMS implanted more frequently than DES. Surgical revascularisation was performed in 60 (13.9%) patients, and medical treatment only was recommended in 32 pa-

Table 2. Angiographic characteristics of in-stent restenosis patients

	Overall	Acute coronary syndrome	Stable angina	P
Artery treated with PCI				0.35
RCA	97 (22.5%)	35 (18.7%)	62 (25.3%)	
LM	19 (4.4%)	7 (3.7%)	12 (4.9%)	
LAD	247 (57.2%)	114 (61.0%)	133 (54.2%)	
Cx	69 (16.0%)	31 (16.6%)	38 (15.5%)	
Lesion type found during primary PCI				
A	124 (28.7%)	59 (31.6%)	65 (26.5%)	0.14
B1+B2	218 (50.5%)	97 (51.8%)	121 (49.4%)	0.14
C	90 (20.8%)	31 (16.6%)	59 (24.1%)	0.14
CTO	52 (12.0%)	11 (5.9%)	41 (16.7%)	0.006
Bifurcation	57 (13.2%)	24 (12.8%)	35 (14.3%)	0.66
Number of stents	1.3 ± 0.5	1.3 ± 0.5	1.3 ± 0.5	0.85
Length of stents	22 ± 11	23 ± 12	22 ± 11	0.55
Diameter of stents	3.2 ± 0.7	3.2 ± 0.5	3.8 ± 0.8	0.81
Restenosis (%)	94 (70–100)	99 (70–100)	90 (30–100)	0.19
Restenosis type according to Mehran				0.98
I	199 (46.1%)	86 (46.5%)	113 (46.1%)	
I A	24 (5.5%)	11 (5.9%)	13 (5.3%)	
I B	85 (19.6%)	36 (19.2%)	49 (20.0%)	
I C	61 (14.1%)	26 (13.9%)	35 (14.3%)	
I D	29 (6.7%)	13 (6.9%)	16 (6.5%)	
II	59 (13.6%)	26 (13.9%)	33 (13.5%)	
III	83 (19.2%)	39 (20.9%)	44 (17.9%)	
IV	91 (21.3%)	36 (19.3%)	55 (22.5%)	

PCI — percutaneous coronary intervention; RCA — right coronary artery, LM — left main coronary artery; LAD — left anterior descending artery; Cx — circumflex artery; CTO — chronic total occlusion

Table 3. Clinical manifestation of restenosis in BMS

Stable angina pectoris	245 (56.7%)
CCS I	13 (3.1%)
CCS II	97 (22.5%)
CCS III	135 (31.1%)
Unstable angina	128 (29.6%)
Braunwald I	8 (1.8%)
Braunwald II	56 (13.0%)
Braunwald III	64 (14.8%)
Myocardial infarction	59 (13.7%)
NSTEMI	31 (7.2%)
STEMI	28 (6.5%)
In-hospital death	10 (2.5%)

CCS — Canadian Cardiovascular Society; STEMI — ST elevation myocardial infarction; NSTEMI — non-ST elevation myocardial infarction

tients (7.4%), with no significant differences between the two groups (Table 4).

The effectiveness of repeated PCI was high in both groups (98.4% among ACS patients *vs* 97.1% among stable angina patients), and angiographic complication were uncommon (4.8% among ACS patients and 1.2% in stable angina patients), mostly comprising side branch occlusions and perforations. The rate of clinical complications (MI, in-hospital death) was also low (3.9%) but higher in ACS patients (6.9% *vs* 1.6%, $p = 0.01$). Five patients with ACS died, all following repeated PCI. The causes of death included cardiac perforation and acute tamponade in one patient, ventricular fibrillation induced during the procedure and not amenable to resuscitation measures in one patient, and severe heart failure due to MI in 3 patients. Overall in-hospital mortality was 1.1% (Table 5).

In multivariate analysis, predictors of ACS as the clinical manifestation of ISR included younger patient age and previous MI. More severe stenosis reduced this risk significantly (Table 6).

DISCUSSION

Restenosis is a problem in interventional cardiology since the very introduction of percutaneous coronary angioplasty. In

Table 4. Further in-stent restenosis management

	Overall (%) (n = 432)	ACS (n = 187)	Stable angina (n = 245)	P
Re-PCI	340 (78.7%)	149 (79.7%)	191 (77.9%)	NS
POBA	193 (56.8%)	86 (46.0%)	107 (43.7%)	NS
BMS	49 (14.4%)	33 (17.6%)	16 (6.5%)	0.01
DES	98 (28.8%)	30 (16.0%)	68 (27.8%)	0.01
CABG	60 (13.9%)	23 (12.3%)	37 (15.1%)	NS
Pharmacotherapy	32 (7.4%)	15 (8.0%)	17 (6.7%)	NS

ACS — acute coronary syndrome; PCI — percutaneous coronary intervention; POBA — balloon angioplasty, BMS — bare metal stent; DES — drug--eluting stent; CABG — coronary artery bypass grafting

Table 5. Complications of coronary angioplasty in the management of in-stent restenosis

	Overall	ACS	Stable angina	P
PCI effectiveness	332 (97.7%)	146 (98.4%)	186 (97.3%)	NS
Angiographic complications	11 (2.5%)	9 (4.8%)*	3 (1.2%)**	0.05
Peripheral embolisation	1	1	0NS	
Acute occlusion	2	1	1	NS
No-reflow	3	3	0	NS
Side branch occlusion	4	3	1	NS
Perforation	4	2	2	NS
Clinical complications	17 (3.9%)	13 (6.9%)	4 (1.6%)	0.01
Myocardial infarction	12 (2.8%)	8 (4.3%)	4 (1.6%)	NS
Death	5 (1.1%)	5 (2.7%)	0	NS

*Both acute occlusion and perforation in 1 patient; **both peripheral embolisation and side branch occlusion in 1 patient; ACS — acute coronary syndrome; PCI — percutaneous coronary intervention

Table 6. Multivariate analysis: risk factors of acute coronary syndrome as the clinical manifestation of in-stent restenosis

Variable	HR	95% CI	P
Age	4.02	1.27–12.69	0.017
Stenosis (%)	2.97	0.82–10.70	0.0097
Previous AMI	0.56	0.34–0.94	0.026

AMI — acute myocardial infarction; CI — confidence interval; HR — hazard ratio

the balloon angioplasty era, restenosis was very common, complicating up to 60% of procedures [1]. Clinical symptoms of restenosis mainly included angina pectoris of increasing severity. Widespread use of BMS resulted in a reduced rate of restenosis, but physicians still widely perceived it as a benign clinical phenomenon [6, 7, 13]. In addition, the rate of restenosis is overestimated in randomised clinical studies. In these studies, angiographic ISR is mainly evaluated, defined as stenosis of more than 50% of the vessel lumen, and follow--up coronary angiographies are obligatory [2–4]. Thus, the rate of angiographic restenosis is much higher than that of symptomatic restenosis, and ACS resulting from ISR is less common in randomised clinical studies compared to routine clinical practice, with hospital admissions of mostly symptomatic patients. However, restenosis is asymptomatic in many cases (10–50%) [14, 15], and most randomised studies focused on angiographic findings and not clinical symptoms of restenosis [6, 7].

Coronary angioplasty induces vessel wall damage and triggers a repair process involving mainly smooth muscle cells, endothelial cells, and inflammatory cells. Restenosis following stent implantation results mainly from neointimal proliferation and extracellular matrix formation, and the severity of these processes is largely related to the severity of vessel wall damage [16–18]. The duration of these processes ranges from several weeks to many months, thus explaining the prevalent view that the clinical symptoms of restenosis, resulting from progressive reduction of vessel lumen, mainly include angina pectoris of increasing severity. For many years, ACS was considered a rare presentation of ISR, with the exception of subacute stent thrombosis [19, 20]. The latter occurs within 1 month from BMS implantation, before stent endothelialisation, and must be distinguished from ISR. However, another underrecognised problem is late thrombosis that results from

Table 7. Acute coronary syndromes as the clinical manifestation of in-stent restenosis in previous studies

Authors	No. of patients	ACS (%)	UA/NSTEMI (%)	STEMI (%)
Bossi et al. (2000) [1]	234	57.2	53.7	3.5
Walters et al. (2002) [21]	191	68	60	8
Assali et al. (2006) [28]	1441	57	–	–
Chen et al. (2006) [29]	984	35.9	33.7	2.2
Nayak et al. (2006) [30]	212	–	5.7*	4.7
Steinberg et al. (2007) [31]	2539	53.3	51.6	1.7
Bainey et al. (2008) [32]	744	70.7	52.2	18.5
De Labriolle et al. (2009) [33]	1958	78.1	76.5	1.6
Bonello et al. (2009) [34]	137	–	62	–

*Only NSTEMI; ACS — acute coronary syndrome; UA — unstable angina; STEMI — ST elevation myocardial infarction; NSTEMI — non-ST elevation myocardial infarction

vessel wall damage and the presence of a foreign body but is also related to different structure of neointima. Patients with restenosis following stent implantation manifest with clinical symptoms earlier than patients after balloon angioplasty [21]. In addition, a thrombus is more often noted within the stent in these patients [22, 23]. Interestingly, these thrombi are seen after more than one month from stent implantation, a period considered to be sufficient for complete BMS endothelialisation. Experimental, autopsy, and histopathological studies of biological specimens retrieved during atherectomy revealed that the neointimal tissue within the stent is rich in tissue factor [24, 25]. This may result in thrombosis on the neointimal surface that completely covers the stent structure, especially when the laminar blood flow is disturbed by the excess tissue. Some intracoronary ultrasonographic studies showed that the neointima may undergo processes similar to atherogenesis, including plaque rupture with resulting vessel occlusion [26]. It is also possible that complete stent endothelialisation may not occur for several months following BMS implantation. Premature cessation of combined antiplatelet therapy may also be a significant factor in these cases [27].

A number of studies focusing on clinical presentation of ISR have been recently published, and the presented data are concordant with our findings. More than half of patients with ISR (33.7–78.1%) are readmitted with symptoms of ACS. The most prevalent presentation in this group is unstable angina pectoris (26.4–60%), but STEMI is also diagnosed in a significant proportion of patients (1.7–4.7%) (Table 7).

Bossi et al. [1] showed that the presence of more severe ISR is associated with a higher risk of repeated revascularisation within one year of the initial PCI (odds ratio [OR] 1.65). In addition, similarly to our study, shorter time from primary PCI to the occurrence of ISR symptoms was associated with a higher risk of revascularisation [13, 19]. This may suggest that early restenosis is related to more aggressive neointimal proliferation, as reflected in findings of histopathological [15, 16] and ultrasonographic [17, 26] studies.

Walters et al. [21] found that independent risk factors of ACS as the clinical manifestation of ISR in univariate analyses included renal failure, small arterial diameter (< 3 mm) and stent length exceeding 20 mm, factors generally favouring restenosis. In addition, ACS was a more frequent clinical manifestation of restenosis in patients following stent implantation compared to restenosis following balloon angioplasty (OR 2.0).

Assali et al. [28] noted that patients with ISR manifesting as ACS had more conventional risk factors of atherosclerosis such as hypertension, diabetes, and tobacco use. These patients were older, more frequently underwent previous coronary artery bypass grafting (CABG), and primary PCI was more commonly performed for acute indications, similarly to our group. Explanation of these findings is not clear and may include larger volume of atherosclerotic plaque, more severe stenosis, the presence of a thrombus, and underestimation of true vessel lumen compared to elective PCI. Younger age and more common previous MI in patients with ACS in our study may suggest more aggressive atherogenesis. During 9-month follow-up in the cited study, patients with ACS were at higher risk of death (2% *vs* 0.5%) and repeated revascularisation (33% *vs* 21%) compared to patients with stable angina.

Chen et al. [29] showed in a multivariate analysis that previous CABG, renal failure, hypertension, beta-blocker use, female gender and low left ventricular ejection fraction were related to more common occurrence of ACS as the clinical manifestation of ISR. Explanation of these findings is largely speculative. Women probably present later with recurrent symptoms and less frequently receive appropriate medications [23]. Renal failure is related to the presence of procoagulant factors and less frequent aggressive treatment of atherosclerotic disease. Previous CABG suggests more advanced coronary artery disease.

Nayak et al. [30] showed than ACS as the clinical manifestation of ISR was more frequently associated with renal failure, ACS at the time of primary PCI and shorter time from the primary PCI. In addition, coronary angiography in patients

with ACS showed more aggressive restenosis, more common complete in-stent occlusion and the presence of thrombus in patients with STEMI. Myocardial infarction occurred 80––90 days following PCI, suggesting that a longer duration of antiplatelet therapy should be considered. The rate of MI was also higher than the commonly observed rate of late ISR (0.4–0.8%) [27–29], suggesting an additional contributing factor of aggressive restenosis with largely reduced blood flow. In our study, the angiographic type of restenosis according to Mehran classification was not found to be significantly related to the clinical manifestation. Perhaps the rate of development and the characteristics of the neointimal tissue are more important than the degree and length of stenosis. In addition, more severe stenosis may favour the development of collateral circulation that may protect from the occurrence of ACS.

Steinberg et al. [31] found that ACS was a more common manifestation of ISR in women and patients with renal failure. However, subsequent prognosis was similarly good in both groups, as patients with ACS did not differ significantly from the other patients in regard to the rate of deaths and recurrent MI at 6-month follow-up, except for patients with MI, in whom mortality was 8.1% compared to 3.1%.

Limitations of the study

Our study has significant limitations. It was a retrospective single-centre analysis. Follow-up coronary angiography after PCI was symptom-driven, thus our study did not include patients with asymptomatic restenosis. Widespread use of DES may limit clinical significance of our findings but these data will still be valid in less wealthy countries and in patients in whom BMS implantation was chosen for various reasons. Our department of cardiology is a reference centre treating most difficult cases, so the rate of ACS may be higher than in an average population. Clopidogrel was widely introduced in the last 3 years, superseding previously used ticlopidine, and it cannot be excluded that clinical manifestations of ISR are less severe with clopidogrel.

CONCLUSIONS

In-stent restenosis after BMS implantation is a serious clinical problem. More than 40% of patients with ISR present with ACS, including 13.7% patients with MI, more frequently among younger patients and patients with previous MI. Most patients with ISR are treated with repeated PCI with high success rate (97.7%), although the risk of clinical complications is considerably higher in patients presenting with ACS.

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Ostry zespół wieńcowy jako częsty objaw restenozy po implantacji stentu klasycznego

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Streszczenie

Wstęp: Restenoza w stencie metalowym (ISR) po zabiegu przezskórnej interwencji wieńcowej (PCI) jest zjawiskiem występującym w 20–30% przypadków. Wprawdzie wprowadzenie stentów powlekanych lekami antyproliferacyjnymi (DES) spowodowało znaczne zmniejszenie częstości implantacji klasycznych metalowych stentów (BMS), ale w wielu krajach europejskich, w tym w Polsce, nadal liczba implantowanych BMS przewyższa liczbę DES. Restenoza często jest postrzegana jako łagodne zjawisko kliniczne, trudne w terapii, ale obarczone niskim ryzykiem powikłań.

Cel: Celem pracy była analiza obrazu klinicznego ISR na podstawie doświadczenia jednego ośrodka.

Metody: Na podstawie bazy angiograficznej Kliniki Kardiologii Uniwersytetu Medycznego w Lublinie przeanalizowano wszystkie przypadki restenozy w stencie metalowym rozpoznane w latach 2000–2007. Wskazaniem do przeprowadzenia kontrolnego badania koronarograficznego był nawrót objawów. Analizie poddano czynniki wpływające na rodzaj prezentacji klinicznej, sposoby dalszego postępowania terapeutycznego i powikłania wewnątrzszpitalne.

Wyniki: Wśród 15 910 angiografii przeprowadzonych w tym okresie rozpoznano 432 przypadki pierwszorazowej restenozy w BMS. Większość spośród chorych (68,3%) stanowili mężczyźni, średnia wieku wyniosła 62 lata (27–86 lat). Objawy kliniczne nawrotu zwężenia wystąpiły średnio po 7 miesiącach od pierwotnego zabiegu PCI. Ostry zespół wieńcowy (ACS) wystąpił u 43,3% osób, w tym: niestabilna dusznica bolesna u 29,6%, NSTEMI u 7,2%, a STEMI u 6,5% chorych. W trakcie hospitalizacji zmarło 5 pacjentów leczonych z powodu ACS, nie odnotowano zgonów w grupie z objawami stabilnej dusznicy bolesnej. W analizie wieloczynnikowej stwierdzono dodatnią korelację między ISR, manifestującą się jako ACS, a przebytym zawałem serca i młodszym wiekiem chorych, natomiast ujemną — z większym stopniem zwężenia tętnicy. Częstość powikłań klinicznych re-PCI (zawał serca, zgon) była wyższa wśród pacjentów z ACS (6,9% *v.* 1,6%).

Wnioski: U ponad 40% chorych z ISR występują objawy ACS, w tym u 13,7% — zawał serca. Takiej prezentacji ISR sprzyja młodszy wiek i przebyty w przeszłości zawał serca. Większość pacjentów z ISR leczy się ponownie za pomocą PCI, którego skuteczność jest bardzo wysoka (97,7%), ale w przypadku ACS związana z większym ryzykiem powikłań klinicznych.

Słowa kluczowe: restenoza, stent klasyczny, ostry zespół wieńcowy

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