In-stent coronary restenosis, but not the type of stent, is associated with impaired endothelial-dependent vasodilatation

Katarzyna Mizia-Stec[1], Zbigniew G sior[1], Maciej Haberka[1], Magdalena Mizia[1], Artur Chmiel[1], Joanna Janowska[2], Micha Holecki[2], Marcin Mielczarek[1], Barbara Zahorska-Markiewicz[2]

[1] Department of Cardiology, Medical University of Silesia, Katowice, Poland

[2] Department of Pathophysiology, Medical University of Silesia, Katowice, Poland

Abstract

Background: Precise mechanisms leading to restenosis are not fully understood. The type of implanted stent and the intensity of atherogenic processes may affects the restenosis rate.

Aim: To compare the long-term effects of the coronary stent implantation – paclitaxel-eluting stent (PES) or bare-metal stents (BMS) – on endothelial-dependent flow-mediated dilation (FMD), platelet-derived growth factor (PDGF) and asymmetric dimethylarginine (ADMA) serum levels and to assess the relationship between FMD, PDGF, ADMA and every-stage in-stent restenosis (eISR).

Methods: The study population included 40 patients with coronary artery disease, who underwent elective percutaneous coronary intervention (PCI) of the left anterior descending artery (LAD) with stent implantation (PES – 21 patients; BMS – 19 patients). Follow-up examination was performed 12 months after PCI.

Results: There were no differences between the PES and the BMS patients regarding FMD (PES: 11.8±7.8%, BMS: 10.5±9.2%), PDGF (PES: 5540±2209 pg/ml, BMS: 4923±2924 pg/ml) and ADMA (PES: 0.474±0.04 µmol/l, BMS: 0.456±0.03 µmol/l) serum levels. The follow-up angiography was performed when clinically indicated in 25 patients: in 15 patients with PES and 10 patients with BMS implanted. The eISR was found in 12 subjects: in 7 (47%) with PES and in 5 (50%) with BMS (NS). In all patients with eISR, the FMD values were significantly lower (6.1±3.5%, p=0.003) compared to the patients without eISR (14.3±7.8%). FMD was the only independent risk factor for eISR (OR=0.631, 95% CI 0.412-0.942, p=0.0003). The cut-off point for FMD ≤8.4% as a parameter predicting eISR was established (p=0.0001, sensitivity: 83.3%, specificity: 92.3%, PPV: 90.9%, NPV: 85.7%).

Conclusions: The type of stent implanted into LAD does not affect the FMD, PDGF and ADMA serum levels assessed one-year after a PCI procedure. The occurrence of an early in-stent restenosis is associated with impaired FMD at the time of one-year follow-up.

Key words: coronary artery disease, PES, BMS, FMD, PDGF, ADMA

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Introduction

Percutaneous coronary intervention (PCI) has become a widespread and effective treatment procedure for patients with coronary artery disease (CAD). However, despite improvement in techniques, devices and experience, in-stent restenosis (ISR) remains a considerable limitation and major challenge for cardiologists. Introduction of drug-eluting stents (DES), including paclitaxel-eluting stents (PES), held a promising strategy for ISR prevention [1]. However, recently published data, the majority of which regarded sirolimus-eluting stents (SES), brought serious doubts about the long-term safety of DES in terms of cardiac deaths and myocardial infarctions [3-5].

Precise mechanisms leading to restenosis are not fully understood. A growing body of evidence suggests that an abnormal vascular wall response to the implanted stent including cytokine activation, local inflammatory state, and smooth muscle cell (SMC) proliferation contribute to excessive growth and restenosis [6]. Previous studies focused on BMS suggested an important role of endothelial dysfunction in the development of ISR [7]. Van Beusekom et al. [8], comparing histology of ISR tissue from BMS and DES, observed a persistent incomplete healing response even 2 years after DES implantation. An increasing number of PCI with DES implantation, novel data on ISR, and disturbing conclusions from the latest studies prompted us to perform an evaluation of

Address for correspondence:

Katarzyna Mizia-Stec MD PhD, Klinika Kardiologii, Śląski Uniwersytet Medyczny, ul. Ziołowa 45/47, 40-635 Katowice, tel.: +48 32 252 39 30, e-mail: kmizia@op.pl

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ultrasonographic and biochemical markers of atherosclerosis in relation to the type of stent implanted.

We aimed to compare the long-term effect of the coronary stent implanted – PES or BMS – on endothelial-dependent flow-mediated dilation (FMD), platelet-derived growth factor (PDGF) and asymmetric dimethylarginine (ADMA) serum levels. The secondary aim of our study was to detect whether FMD, PDGF and ADMA levels are related to the outcome of the study population – every-stage ISR (eISR).

Methods

Study group

We enrolled 40 consecutive patients (all males: mean age 58.8±9.8 years) who had undergone a PCI procedure with stent implantation into a proximal lesion in the left anterior descending artery (LAD) at least 8 months earlier (range: 8-14 months): 21 patients with DES (PES) and 19 patients with BMS. Percutaneous interventions were performed between September 2005 and March 2006, according to the European Society of Cardiology (ESC) and Polish Cardiac Society guidelines [9, 10]. The final decision regarding the type of stent implanted (DES or BMS) was made by the operator according to the ESC-approved British Institute NICE recommendations for DES implantation [10].

The exclusion criteria included: evidence of present or recent (previous 3 months) infectious disease, fever, immune disorders, immunosuppressive therapy, malignancy, and ECG abnormalities that would hamper ST-segment analysis (LBBB, paced rhythm, atrial fibrillation, WPW syndrome). Detailed physical examination, ENT and gynaecology consultations, chest X-ray and erythrocyte sedimentation rate were taken into consideration to exclude acute or chronic inflammation of organs outside the circulatory system.

The clinical characteristics of the patients included: medical history (familial disease, concomitant disease, pharmacotherapy used, smoking status, alcohol and caffeine consumption, data on major cardiovascular events during the period following PCI-LAD), physical examination (arterial pressure, body mass index, and waist-hip ratio), laboratory tests (lipidogram), accessory investigations (electrocardiogram, echocardiography), and detailed characteristics of therapy used.

The subjects were instructed to fast overnight, avoid smoking for 24 hours prior to the examination, and not take medication that could potentially modify measurement results, e.g., nitrates, calcium channel blockers. The study was approved by the local Ethics Committee, and all patients gave written informed consent prior to enrolment.

Percutaneous coronary interventions

The PCI was performed with conventional techniques by a femoral approach. Procedural success defined as a reduction of stenosis to <30% residual narrowing with an improvement of angina symptoms and without major in-hospital complications was achieved in all patients. No patient had significant side-branch closure during the procedure. There were no differences in the lesion and procedural parameters between the PES and the BMS groups regarding: type of lesion (A/B1 vs. B2/C, according to the ACC), stent diameter, direct stenting, stent deployment pressure, frequency of multivessel disease, multi-lesion intervention, and number of stents implanted (Table I). The stent length in PES was significantly longer than in BMS (23.5±6.6, 17.9±5.9, respectively; p=0.05).

Aspirin (100 mg/d) was prescribed to all patients; thienopyridine (ticlopidine 250 BID or clopidogrel 75 mg daily) was continued for at least 4 weeks after intervention (patients with DES received thienopyridine for at least 9 months).

Repeated elective coronary angiography

Repeated elective coronary angiography was performed when clinically indicated (angina symptoms, positive exercise test). At re-angiography multiple views were obtained, and ISR was assessed by quantitative

Table I. Comparison of lesion and procedural variables obtained at the time of PCI procedure in the PES and BMS groups

Lesion and procedural variables	PES n=21	BMS n=19	p
Lesion type B2/C [%]	61.9	57.9	NS
Stent length [mm, mean ± SD]	23.5±6.6	17.9±5.9	0.05
Stent diameter [mm, mean ± SD]	2.99±0.3	3.15±0.6	NS
Stent deployment pressure [atm, mean ± SD]	12.8±3.5	12.8±1.1	NS
Multivessel disease [%]	67.0	79.0	NS
Multi-lesion intervention [%]	19.0	15.8	NS
Number of stents [mean ± SD]	1.19±0.4	1.16±0.4	NS

Abbreviations: LAD – left anterior descending artery

methods. Measurements were performed with TCS Symphony 2.02 Medcon INC by one operator. The data of CAD progression defined as eISR and/or progression outside of the implanted stent (a critical lesion not observed previously) were also analysed.

Blood sampling and laboratory measurements

Measurements of PDGF and ADMA were carried out with commercial kits: 6-8 ml samples of venous blood were collected from each subject after an overnight fast. After clot formation, the samples were centrifuged (1000 g) at 2-8°C for 10 minutes. The obtained serum was drawn into plastic vials, and stored at –80°C until the time of assay.

The measurements of human PDGF-BB were done by enzyme-linked immunosorbent assay kits (ELISA) (R&D Systems, Cambridge, USA). The sensitivity of PDGF assay was less than 31.2 pg/ml. Intra- and inter-assay coefficients of variations (CV) were <4.5% and <7.6% respectively.

The measurements of ADMA were performed using the ADMA ELISA Kit (Immundiagnostik AG, Bessheim, Germany). The sensitivity of ADMA assay was less than 0.05 µmol/l. Intra- and inter-assay CVs were <10% and <7.5% respectively.

Lipid parameters (serum cholesterol, HDL cholesterol, LDL cholesterol, triglycerides) were obtained using routine laboratory methods.

Flow-mediated dilatation (FMD)

The measurements of brachial artery FMD were done in a quiet, temperature-controlled room, between 9 and 11 am. Patients were examined after at least a 10-minute rest; ultrasound examination was performed in a supine position.

Experienced investigators took measurements in a B-mode presentation using a high frequency ultrasound system (Toshiba Aplio) equipped with vascular software for two-dimensional (2D) imaging, colour and spectral Doppler, an internal electrocardiogram monitor and a high frequency vascular transducer (multiple-frequency: 7-10 MHz).

The brachial artery of the dominant forearm was visualised above the antecubital fossa in a longitudinal plane, with a sphygmomanometric cuff on the proximal portion of the arm. The brachial artery diameter was described as a minimal distance between 'm' lines, from the anterior to posterior wall of the artery. Images were acquired with ECG gating, with measurements made in end diastole, which corresponds to the onset of the R wave.

The study was performed in three stages: 1) Stage 1: baseline brachial artery diameter and flow measurements were taken, and the average was calculated for each subject; 2) Stage 2: the sphygmomanometer cuff was inflated to 200 mmHg to occlude arterial inflow for 3 min; 3) Stage 3: brachial artery diameter and blood flow were measured and the mean of the values obtained during fifty to sixty seconds after cuff deflation was calculated.

Taking these two measurements into consideration (baseline and after cuff deflation), FMD (%) was calculated (percent increase of the artery diameter in comparison to baseline results).

After a 10-minute rest, a sublingual tablet of nitroglycerin (0.5 mg) was administered to determine the maximum obtainable exogenous vasodilatory response. Brachial artery diameter and blood flow were measured following NTG, and NTG-mediated dilatation (NMD) was determined.

Statistical analysis

The results are expressed as means ± SD. The results were analysed with the ANOVA test, including Newman-Keuls correction. Clinical parameters and the results of performed tests were compared using the Chi square test for proportions with Yates correction, the two-sample t-tests for normally distributed continuous variable (Student's t-test preceded by Fisher's test); in case of abnormal distribution, the Mann-Whitney U test was used. Spearman's rank correlation test was applied to assess relations between variables. Stepwise multivariate analysis was performed with ADMA as the dependent variable. Independent predictors of eISR were calculated by logistic regression. The ROC (receiver operator characteristic) curve analysis was performed and the cut-off point for a parameter predicting eISR with the highest sensitivity and specificity was established. A value of $p < 0.05$ was considered statistically significant. All analyses were performed using the MedCalc 9.0 software.

Results

Clinical characteristics

No significant differences were found in clinical parameters between the PES and BMS groups (Table II).

The pharmacotherapy used was also similar: aspirin – 100/100%; thienopyridine – 52/37%, beta-blockers – 86/100% (metoprolol, bisoprolol); calcium channel blockers – 24/21%, statins (simvastatin, atorvastatin) – 81/68%; inhibitors of angiotensin-converting enzyme – 81/85%, nitrates – 43/26% (PES/BMS respectively).

Major cardio-vascular events during the period following PCI-LAD occurred in 2 (9.5%) patients with PES and in 2 (10.5%) patients with BMS, and consisted of CAD progression with symptomatic stenosis requiring revascularisation. There were no deaths, strokes or myocardial infarctions (MI) after PCI.

Results of repeated coronary angiography

Repeated coronary angiography was performed in 25 patients: 15 patients of the PES (PES subgroup) and 10 patients of the BMS (BMS subgroup) groups. CAD progression defined as eISR and/or progression outside of the implanted stent (a critical lesion not observed previously) was found in 9 subjects of the PES subgroup (60%: eISR in 7 patients; progression outside of the

Table II. Comparison of clinical variables and serum lipids in the PES and BMS groups

	PES n=21	BMS n=19	p
Age [years, mean ± SD]	56.2±10.3	60.5±9.1	NS
BMI [kg/m^2, mean ± SD]	28.9±4.4	29.6±4.0	NS
WHR	1.00±0.07	1.03±0.05	NS
Hypertension [%]	71	84	NS
Diabetes mellitus [%]	24	21	NS
Current smoker [%]	24	18	NS
Prior myocardial infarction [%]	33	58	NS
LVEF [%]	56.9±7.9	56.0±10.2	NS
CCS class 1-2 [%]	43	37	NS
Serum lipid parameters			
Total cholesterol [mg/dl, mean ± SD]	183.0±32.2	199.7±54.9	NS
LDL cholesterol [mg/dl, mean ± SD]	107.7±27.8	95.8±33.1	NS
HDL cholesterol [mg/dl, mean ± SD]	42.1±10.6	42.1±8.6	NS
Triglycerides [mg/dl, mean ± SD]	165.3±76.1	208.4±78.6	NS

Abbreviations: BMI – body mass index, WHR – waist-to-hip ratio, LVEF – left ventricular ejection fraction, CCS – Canadian Cardiac Society

implanted stent in 6 patients) and in 6 subjects of the BMS subgroup (60%: eISR in 5 patients; progression out of the implanted stent in 3 patients) (NS).

The eISR (any reduction of the luminal diameter) was found in 7 (47%) patients of the PES subgroup (range of eISR: 30-70%; ISR 350% in 3 patients) and in 5 (50%) patients of the BMS subgroup (range of eISR: 39-70%; ISR 350% in 4 patients) (NS).

PDGF and ADMA levels

There were no significant differences between serum PDGF and ADMA levels in the PES and BMS groups (Table III).

In all patients examined, ADMA serum levels significantly correlated with: CCS class (r= –0.217), LVEF (r=–0.325), previous MI (r=0.295, p <0.05), age (r=–0.236, p <0.05), and current smoking (r=0.333, p <0.05). In a multivariate logistic regression analysis, LVEF (p=0.02) and current smoking (p=0.02) independently influenced ADMA serum levels (r=0.488). This association was independent of age, CCS class, previous MI, WHR, total cholesterol, and FMD.

There were no significant correlations between serum PDGF levels and the clinical variables.

Flow-mediated dilatation

The FMD was comparable between the PES and BMS groups. The study groups did not differ as to the brachial artery diameters and NMD values (Table III). There were no significant correlations between the FMD and clinical variables.

Comparison of subjects with and without eISR in repeated coronary angiography

Patients with and without eISR had comparable clinical characteristics, including age, BMI, WHR, coronary risk

Table III. Mean PDGF, ADMA serum levels and FMD, NMD values in the PES and BMS groups

	PES n=21	BMS n=19	p
PDGF [pg/ml]	5540.2±2209.3	4923.0±2924.8	NS
ADMA [µmol/l]	0.474±0.04	0.456±0.03	NS
FMD			
BAd baseline value [mm]	4.48±0.41	4.28±0.84	NS
FMD [%]	11.8±7.8	10.5±9.2	NS
NMD			
BAd baseline value [mm]	4.30±0.59	4.42±0.70	NS
NMD [%]	17.54±8.5	20.5±16.8	NS

Abbreviations: ADMA – asymmetric dimethylarginine, BAd – brachial artery diameter, FMD – endothelial-dependent flow-mediated dilation, NMD – nitroglycerin-mediated dilatation, PDGF – platelet-derived growth factor

factors (systemic hypertension, diabetes, smoking status), and left ventricular systolic function (Table IV). Chest pain class 1-2 according to CCS class occurred more frequently in patients with eISR (Table IV). Patients with or without eISR also did not differ in terms of pharmacotherapy used.

Analysis of serum lipids revealed significantly higher HDL-Ch serum levels in the eISR subgroup as compared to the subjects without eISR. There were no differences in TCh, LDL-Ch, TG serum levels.

Characteristics of LAD intervention showed a significant difference in stent deployment pressure, which was lower in the eISR subgroup (p=0.04) (Table IV). Lesion type, stent length and stent diameter were comparable in the subgroups with and without eISR.

There were no significant differences between serum PDGF and ADMA levels in patients with or without eISR (Table IV).

The mean FMD value was significantly lower in the eISR subgroup as compared to the subjects without eISR (p=0.003) (Table IV). The regression analysis revealed a negative correlation between the degree of eISR and the FMD values (r=–0.340, p=0.047) (Figure 1). In univariate and stepwise multivariate logistic regression analysis FMD was the only independent risk factor for eISR (OR=0.631; 95% CI 0.412-0.942; p=0.0003). This association was independent of age, diabetes mellitus, systemic hypertension, TCh, smoking status, type of lesion, stent length, stent diameter, and stent deployment pressure. The cut-off point for FMD as a parameter predicting eISR was established – FMD ≤8.4% suggesting eISR (p=0.0001, sensitivity 83.3%, specificity 92.3%, PPV – 90.9%, NPV – 85.7%; area under the ROC curve – 0.891) (Figure 2). When considering the above-mentioned cut-off point for FMD (8.4%), 1 (7.7%) out of 13 patients without eISR versus 10 (83%) of 12 patients with eISR had FMD ≤8.4% (Figure 2).

Discussion

Our study was performed in a selected population – male patients treated with PCI of LAD lesion with stent implantation, PES or BMS, within one year after the procedure. We aimed to compare the long-term effects of

Table IV. Comparison of subjects with and without every-stage in-stent restenosis (eISR) in controlled coronary angiography

	eISR (+) subgroup n=12	eISR (–) subgroup n=13	p
PES/BMS	7/5	8/5	NS
Clinical variables			
Age [years, mean ± SD]	56.8±12.1	56.4±9.1	NS
BMI [kg/m^2, mean ± SD]	27.3±4.5	30.8±4.0	NS
WHR [mean ± SD]	1.00±0.07	1.02±0.06	NS
Systemic hypertension [%]	75	61.5	NS
Diabetes mellitus [%]	16.7	30.8	NS
Current smoker [%]	33.3	15.4	NS
Prior myocardial infarction [%]	25	46.2	NS
LV EF [%, mean ± SD]	57.4±4.6	53.4±7.5	NS
CCS 1/2 [%]	58.5	23.1	0.03
Serum lipids			
Total cholesterol [mg/dl, mean ± SD]	195.8±41.4	193.1±53.2	NS
LDL cholesterol [mg/dl, mean ± SD]	107.1±37.6	104.6±26.7	NS
HDL cholesterol [mg/dl, mean ± SD]	47.0±8.7	37.5±8.8	0.041
Triglycerides [mg/dl, mean ± SD]	195.1±91.2	187.4±77.8	NS
LAD intervention (PCI + stent)			
Lesion type B2/C [%]	66.7	53.8	NS
Stent length [mm, mean ± SD]	20.3±5.5	20.8±8.5	NS
Stent diameter [mm, mean ± SD]	3.14±0.3	2.97±0.5	NS
Stent deployment pressure [atm, mean ± SD]	12.9±2.1	15.0±2.8	0.04
PDGF [pg/ml, mean ± SD]	5089.9±2257.3	5840.4±2479.1	NS
ADMA [µmol/l, mean ± SD]	0.476±0.03	0.473±0.04	NS
FMD			
BAd baseline value [mm, mean ± SD]	4.46±0.68	4.25±0.43	NS
FMD [%, mean ± SD]	6.12±3.5	14.3±7.8	0.003
NMD			
BAd baseline value [mm, mean ± SD]	4.32±0.61	4.40±0.72	NS
NMD [%, mean ± SD]	20.15±8.5	18.1±9.1	NS

Abbreviations: as in Tables II and III

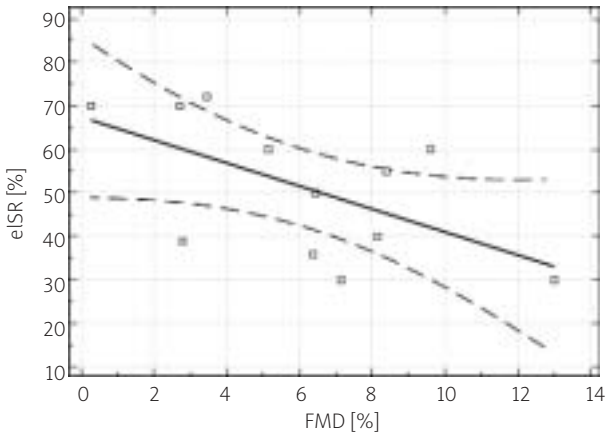

Figure 1. Correlation between flow-mediated dilatation (FMD) and every-stage in-stent restenosis (eISR) (r=–0.340, p=0.047)

the coronary stent implanted on ultrasonographic and biochemical markers of endothelial dysfunction and atherosclerosis. The study would indirectly add to the explanation of increased risk of adverse clinical events in patients with DES implantation. However, our results do not support this hypothesis. Endothelial dysfunction assessed by FMD was comparable in the two study groups. Moreover, biochemical parameters of endothelial dysfunction were also comparable.

The PDGF is a cytokine produced by endothelium and thrombocytes taking part in the activation of the inflammatory and aggregation processes. The PDGF's influence on atherosclerosis development has not been determined unambiguously. Some authors suggest its cardioprotective effect [11, 12]. Nevertheless, the data on a positive correlation between adverse outcomes of invasive procedures in CAD and higher expression of inflammatory markers, including PDGF, prevail. The elevated serum concentration of PDGF, while inducing the migration and proliferation of smooth muscle cells and hyperplasia of intima, particularly in concurrence with decreased fibrinolytic activity of serum, is considered a major risk factor for restenosis [13]. The use of numerous methods to lower PDGF activity correlates with a significant reduction of restenosis occurrence after PCI and stenting [14-17]. In our study population PDGF serum levels were not related to the type of stent implanted and occurrence of ISR.

The ADMA inhibits NO synthesis by NO synthase, leading to endothelial dysfunction. It has been shown to be one of the strongest risk predictors of cardiovascular events in patients with stable CAD [18, 19]. Interestingly, even a small elevation of ADMA is correlated with increased cardiovascular risk. According to Krempl et al. [20] ADMA serum concentration is elevated in unstable angina. Circulating ADMA leads to an increased resting vascular tone and exaggerates some pro-atherogenic mechanisms, including platelet adhesion and aggregation, proliferation of VSMC and extracellular matrix formation [21-23]. Data in literature on ADMA assessment in patients undergoing PCI are limited. There is only a study by Lu et al. [24] showing the increased risk for major cardiovascular events in patients with elevated plasma ADMA after PCI in stable CAD. The relative risk for cardiovascular events increased by 36% when plasma ADMA levels increased

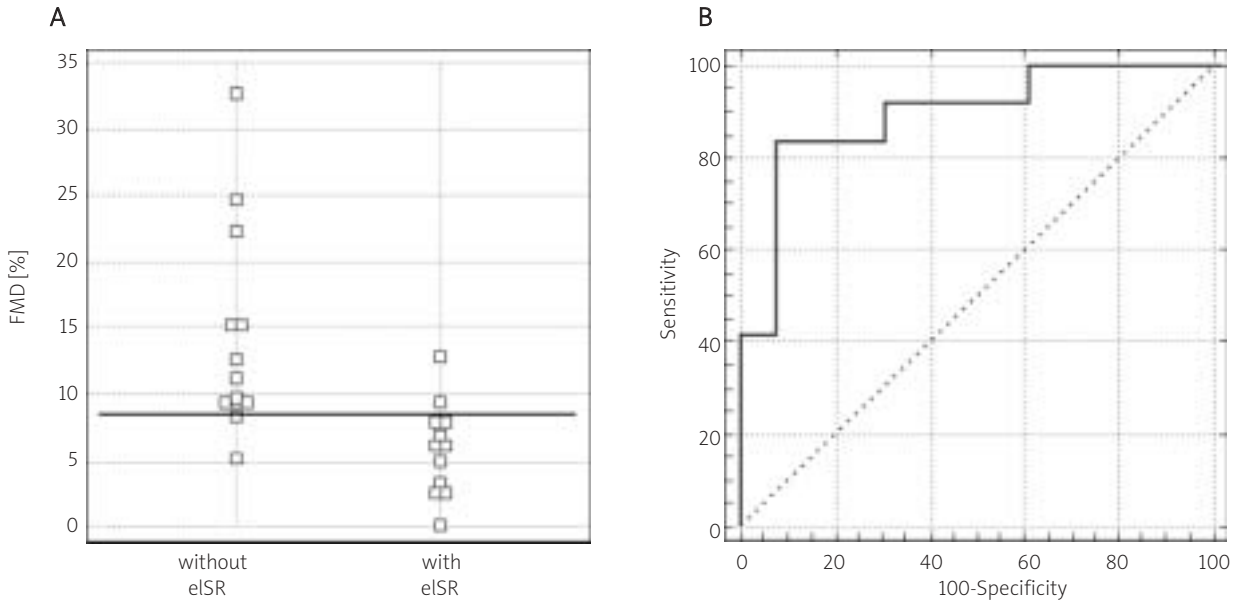

Figure 2. A – Flow-mediated dilatation (FMD) values in subgroups with or without every-stage in-stent restenosis (eISR); **B** – ROC curve for FMD as a predictor of eISR

by 0.1 µmol/l. In our study ADMA serum levels were comparable between study groups and the range of observed values was relatively narrow.

In summary, general vascular status of the study group represented by functional and biochemical parameters did not differentiate the patients with DES and BMS implanted.

On the other hand, our findings support previously published data on systemic endothelial dysfunction observed in cases with restenosis [8, 25, 26].

Despite limitation in the study population number, we showed a close relationshio between restenosis and impaired FMD values. While previous studies recognised only clinically relevant ISR events described as in-stent stenosis 350% [8, 27], in our study all restenoses independently of the degree in quantitative angiography (ranging between 30 and 72%) were assessed. The presented findings suggest that early stages of restenosis are associated with endothelial dysfunction and impaired FMD may be useful for such early ISR identification.

Our results are in accordance with those observed by Kitta et al. [8]. The authors found that impairment of FMD at the time of 6-month follow-up was independently associated with late ISR (350%) in native coronary arteries, whereas baseline FMD did not show such an association. In the study by Patti et al. [27] impaired FMD assessed 30 days after PCI independently predicted occurrence of ISR at the six-month follow-up. Similarly to our findings, only patients with clinical indications were subjected to coronary angiography.

Considering the decreased rate of ISR in patients with DES compared to BMS observed in large trials [2], the similar prevalence of eISR documented in our study seems controversial. These results might be in part explained by the limited number of patients and including in the final ISR rate all degrees (not only 350%) of stent restenosis.

In conclusion, the present study showed that PES implantation did not have a negative effect on brachial endothelium-dependent dilatation as well as PDGF and ADMA levels compared to BMS implantation at one year after successful, elective PCI in LAD. The occurrence of an early diameter loss and eISR were associated with impaired FMD at the time of follow-up. Despite a potential role of PDGF and ADMA in restenosis pathomechanisms, our study did not reveal substantial differences between PDGF and ADMA levels in patients with and without eISR. Further studies involving larger study populations will verify the presented data.

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Zjawisko restenozy w stencie, a nie typ implantowanego stentu wieńcowego wiąże się z upośledzeniem wazodylatacji indukowanej przepływem

Katarzyna Mizia-Stec[1], Zbigniew G sior[1], Maciej Haberka[1], Magdalena Mizia[1], Artur Chmiel[1], Joanna Janowska[2], Micha Holecki[2], Marcin Mielczarek[1], Barbara Zahorska-Markiewicz[2]

[1] Klinika Kardiologii, l ski Uniwersytet Medyczny, Katowice

[2] Katedra i Zak ad Patofizjologii, l ski Uniwersytet Medyczny, Katowice

Streszczenie

Cel: Porównanie odleg ego wp ywu rodzaju implantowanego stentu wie cowego [stenty uwalniaj ce paklitaksel (ang. *paclitaxel-eluting stents*, PES) *vs* stenty metalowe (ang. *bare-metal stents*, BMS)] na zale n od ródb onka wazodylatacj indukowan przep ywem (ang. *flow-mediated dilation,* FMD), na st enia p ytkopochodnego czynnika wzrostu (ang. *platelet-derived growth factor*, PDGF) i asymetrycznej dimetylargininy (ang. *asymmetric dimethylarginine*, ADMA) w surowicy krwi oraz ocena zwi zku FMD, PDGF i ADMA z obserwowan po roku od zabiegu restenoz w stencie (ang. *every-stage in-stent restenosis*, eISR).

Metody: Badaniami obj to cznie 40 osób z chorob wie cow po przebytym zabiegu elektywnej angioplastyki przedniej t tnicy zst puj cej z implantacj stentu (PES – 21 chorych, BMS – 19 chorych). Badania kliniczne, w tym FMD i oznaczenie st e PDGF, ADMA w surowicy krwi przeprowadzano po roku od zabiegu.

Wyniki: Nie stwierdzano znamiennych ró nic pomi dzy badanymi grupami (PES i BMS) w zakresie FMD (PES: 11,8±7,8%, BMS: 10,5±9,2%), PDGF (PES: 5540±2209 pg/ml, BMS: 4923±2924 pg/ml) i ADMA (PES: 0,474±0,04 μmol/l, BMS: 0,456±0,03 μmol/l) w badanych grupach. Po uwzgl dnieniu wskaza klinicznych u 25 badanych, w tym 15 chorych z grupy PES i 10 chorych z grupy BMS, wykonano kontroln koronarografi . Wyst pienie eISR stwierdzono u 12 chorych: 7 z PES (47%) i 5 z BMS (50%). U wszystkich badanych z eISR warto ci FMD by y znamiennie ni sze (6,1±3,5%, p=0,003) w porównaniu z badanymi bez eISR (14,3±7,8%). Warto FMD by a jedynym niezale nym czynnikiem ryzyka eISR (OR=0,631; 95% CI 0,412–0,942; p=0,0003). Punkt odci cia dla FMD jako parametru wskazuj cego na eISR wynosi ≤8,4% (p=0,0001; czu o – 83,3%; specyficzno – 92,3%; PPV – 90,9%, NPV – 85,7%).

Wnioski: Typ implantowanego stentu nie ma istotnego wp ywu na warto ci FMD oraz st enia PDGF i ADMA w surowicy obserwowane po roku od elektywnej angioplastyki przedniej t tnicy zst puj cej. Obecno restenozy w stencie zwi zana jest z upo ledzonym FMD po roku obserwacji.

S owa kluczowe: choroba wie cowa, PES, BMS, FMD, PDGF, ADMA

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Adres do korespondencji:

dr hab. n. med. Katarzyna Mizia-Stec, Klinika Kardiologii, Śląski Uniwersytet Medyczny, ul. Ziołowa 45/47, 40-635 Katowice,

tel.: +48 32 252 39 30, e-mail: kmizia@op.pl

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