Clinical and Stent-related Risk Factors for Recurrent Angina After Successful Percutaneous Coronary Intervention

VIOLETA DINESCH[1]*, MIHAIL DINESCH[2], MIRCEA BURUIAN[3]

[1]University of Medicine and Pharmacy, Department of Internal Medicine M3, 38 Gheorghe Marinescu Str., 540139, Tirgu Mures, Romania

[2]Department of Cardiology, Institute for Cardiovascular Disease and Heart Transplant, 50 Gheorghe Marinescu Str., 540136, Tirgu Mures, Romania

[3] University of Medicine and Pharmacy, Department of Morphologic Sciences M,38 Gheorghe Marinescu Str., 540139, Tirgu Mures, Romania

We evaluated the clinical and stent-related risk factors for recurrent angina (RA) symptoms after percutaneous coronary intervention (PCI), as identifying and treating them could improve patient outcomes. We retrospectively analysed patients readmitted at our clinic after successful PCI; 147 (81.66%) patients were hospitalised for RA. Advanced age was associated with RA symptoms. Drug-eluting stents used at the index PCI, especially in small coronary arteries, seemed protective against RA symptoms. In-stent restenosis, which was associated with RA, was more frequent in bare-metal stents than in drug-eluting stents. Further studies are needed to identify other potential risk factors for RA and to determine how to positively influence the evolution of known risk factors.

Keywords: recurrent angina, percutaneous coronary intervention, drug-eluting stent, bare-metal stent

Coronary artery disease (CAD) is one of the leading causes of morbidity and mortality worldwide. Percutaneous coronary intervention (PCI) with stenting has markedly changed the treatment of CAD, becoming the most commonly used myocardial revascularisation method. The evolution in the design and composition of the stent platforms of bare-metal stents (BMS), and the development of drug-eluting stents (DES) coated with antiproliferative drugs to reduce the neointimal hyperplasia responsible for in-stent restenosis (ISR), were stages in the progress of interventional cardiology. Recurrent angina (RA) after a successful PCI raises questions about the prognosis of the patient. Our study aimed to evaluate the clinical and PCI-related risk factors for RA, as their identification and adequate treatment could influence patient outcomes.

Experimental part

We retrospectively included post-PCI patients readmitted at the Adult Cardiology Clinic at the Institute of Cardiovascular Diseases and Transplantation Tirgu Mures from January 2012 to December 2015. We compared the following parameters between the groups with (stable/unstable angina, ST/non-ST elevation myocardial infarction) and without (cardiological reassessment without symptomatology) RA: sociodemographic (age, sex), cardiovascular risk factors (hypertension, smoking, diabetes mellitus, obesity, hypercholesterol-aemia), results of coronarography performed pre-PCI and at readmission, details of the index PCI (type of stent used, localisation in the coronary artery), and type of medication used at the time of readmission (single or dual antiplatelet therapy, statin).

The acquired data were analysed using STATA (version 14.0, Stata Corporation, College Station, TX, USA) and R (version 3.3.3, R Foundation for Statistical Computing, Vienna, Austria). Continuous variables are expressed as mean ± standard deviation and were compared using the t-test. Categorical variables are expressed as frequency and proportions and were compared using contingency tables, the chi-square test, and Fisher's exact test. $p<0.05$ was considered statistically significant. The study design was approved by the institutional ethics review board, and all patients provided informed consent.

Results and discussions

The study included 180 patients, of which, 147 (81.66%) were readmitted for RA. The mean duration of follow-up was 30.97 ± 31.84 months for the RA group and 24.33 ± 35.12 months for the Non-RA group (odds ratio [OR] 0.99, p = 0.298). The baseline demographics and clinical characteristics of the patients are shown in table 1.

Parameter	RA group	Non-RA group	p
Age, years	62.58 ± 10.04	58.87 ± 9.25	0.053
Male	109 (74.14)	27 (81.81)	0.354
Hypertension	139 (93.9)	29 (90.6)	0.237
Diabetes mellitus	34 (23.12)	6 (18.18)	0.537
Hypercholesterolaemia	75 (50.7)	12 (37.5)	0.128
Smoke	20 (13.5)	4 (12.5)	0.79
Obesity	41 (27.89)	10 (30.3)	0.781

Data are expressed as number (%) or as mean ± SD.

Table 1
BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS OF THE PATIENTS WITH AND WITHOUT RA

* email: doc_violeta@yahoo.com

Most patients in both groups benefited from BMS at the index PCI, with additional BMS in the RA group, but without statistical significance between the RA and Non-RA groups (table 2).

Table 2
STENT TYPE USED AT THE INDEX PCI

Parameter	BMS	BMS + DES	DES	p
RA group	104 (70.74)	12 (8.16)	31 (21.08)	0.14
Non-RA group	16 (48.48)	7 (21.21)	10 (20.3)	

Data are expressed as number (%).

An interesting, but not unexpected observation was noted in relation to stent localisation in the coronary artery at the index PCI. Although the left-anterior-descending-artery localisation of BMS was similarly predominant in both groups, the localisation of DES in the small coronary arteries was associated with the Non-RA group (table 3).

LMCA- left main coronary artery, LAD- left anterior descending artery, RCA- right coronary artery, LCX- left circumflex coronary artery

One-third of patients required revascularisation for ISR. Although the presence of ISR was statistically associated with RA and BMS-ISR was more common than DES-ISR (p = 0.009), ISR localisation at the DES or BMS level was not associated with any of the study groups (table 4).

By comparing the patients with DES-ISR and those with BMS-ISR, the presence of a greater number of lesions at a distance from the stent was significantly related to BMS-ISR (table 5).

Parameter		RA group	Non-RA group	p
BMS		116 (78.91)	23 (69.69)	0.25
BMS localisation	LMCA	2 (1.36)	0	0.5
	LAD	76 (51.7)	12 (36.36)	0.06
	RCA	36 (24.48)	8 (24.24)	0,13
	LCX	25 (17)	5 (15.15)	0.87
	Other coronary artery	18 (12.24)	5 (15.15)	0.76
DES		43 (29.25)	16 (48.48)	0.033
DES localisation	LMCA	5 (3.4)	1 (3.03)	0.91
	LAD	26 (17.68)	8 (24.24)	0.542
	RCA	12 (8.16)	5 (15.15)	0.07
	LCX	15 (10.2)	1 (3.03)	0.635
	Other coronary artery	4 (2.72)	5 (15.15)	0.004

Data are expressed as number (%)

Table 3
STENT LOCALISATION AT THE INDEX PCI

Parameter	RA group	Non-RA group	p
ISR alone	23 (15.65)	3 (9.09)	0.421
ISR + native coronary stenosis	25 (17.01)	2 (6.06)	0.175
ISR (accumulated)	48 (32.65)	5 (15.15)	0.046
DES-ISR	6 (40.81)	0	0.594
BMS-ISR	42 (28.57)	5 (15.15)	0.113
Native coronary stenosis alone	70 (47.62)	16 (48.48)	0.928
No native coronary stenosis	29 (19.73)	12 (36.36)	0.039

Data are expressed as number (%)

Table 4
RESULTS OF CORONAROGRAPHY AT READMISSION

STEMI- ST-elevation myocardial infarction, LMCA- left main coronary artery, LAD- left anterior descending artery, RCA- right coronary artery, LCX- left circumflex coronary artery, DAPT- dual antiplatelet therapy

Recurrent angina after PCI is a frequent clinical outcome with a high economic burden [1]. Our study aimed to identify the impact of clinical and PCI-related factors on the development of post-PCI RA. Advanced age was a clinical risk factor for RA. DES utilisation, particularly in small coronary arteries, seemed to be protective against RA. ISR, which was associated with RA, occurred more frequently with BMS than with DES. Comparing DES-ISR and BMS-ISR, only the presence of a higher number of stenoses in the native coronary artery was associated with BMS-ISR.

Advanced age is a common predictor of the development of cardiovascular pathology because it is linked with a greater prevalence of cardiovascular risk factors and comorbidities. Go et al demonstrated a double prevalence of angina symptoms in the 60 to 79-years age group compared to the 40 to 59-years age group [2]. In post-PCI patients, Gaglia Jr. et al showed in a study, within 1-year post-PCI, that increasing age was associated with less post-PCI angina [3]. Contrarily, advanced age was a predictor of RA symptoms compared to the asymptomatic patients in our study.

Data from the literature support the hypothesis of a higher prevalence of adverse outcomes after PCI in the female sex [4-5]. However, in our study, there were no between-sex differences in post-PCI pathology. This is explicable from several points of view. First, there was no recorded

Table 5
DES-ISR vs. BMS-ISR

Parameter		DES-ISR 5 (11.3)	BMS-ISR 48 (88.7)	p
Age, years		67 ± 6.98	61.45 ± 0.75	0.224
Male		5 (83.33)	37 (78.72)	0.793
Hypertension		6 (100)	45 (95.74)	0.606
Diabetes mellitus		3 (50)	12 (25.53)	0.456
Smoke		1 (16.66)	5 (10.63)	0.276
Obesity		1(16.66)	9 (19.14)	0.865
Hypercholesterolaemia		2 (33.33)	23 (48.93)	0.471
Symptomatology	STEMI	0	5 (10.63)	1
	Unstable angina	3 (50)	12 (25.53)	0.334
	Stable angina	3 (50)	25 (53.19)	0.609
	Cardiological reassessment	0	5 (10.63)	1
Stents number/patient		1.17 ± 0.4	1.49 ± 0.77	0.325
Native coronary stenosis	LMCA	0	1 (2.12)	0.71
	LAD	0	10 (21.27)	0.21
	RCA	1 (16.6)	11 (23.4)	0.7
	LCX	0	6 (12.76)	0.353
	Other coronary artery	0	11 (23.4)	0.183
Number of native coronary stenosis/patient		0.17 ± 0.4	0.74 ± 0.82	0.017
Medication	Aspirin	3 (50)	16 (34.04)	0.443
	DAPT	2 (33.33)	29 (61.7)	0.184
	Statin	4 (66.66)	35	0.683

Data are expressed as number (%) or as mean ± SD.

post-PCI mortality, which is higher for women than for men. Second, the incidence of primary PCI, which has a greater potential for complications, was lower in the women. Third, the small proportion (24%) of female patients in this study may have been a limitation in our analysis.

Smoking is a known cardiovascular risk factor in those over 50 years of age, and the benefits of smoking cessation are recognised even in the DES era [6]. In a study involving 2765 patients, Jang et al demonstrated that post-PCI smokers continued to have a higher incidence of angina episodes and a poorer quality of life compared to non-smokers [7]. A small percentage (13.3%) of the patients in our study were active smokers at the time of post-PCI hospitalisation, but this did not significantly influence the post-PCI evolution of RA symptoms. However, our study did not investigate the differences in the smoking intensity of smokers/former smokers and the time since the cessation of smoking.

Although present in higher percentages in the RA group, none of the other cardiovascular risk factors attained statistical significance. Our findings may be the consequence of good control for these risk factors or due to the few number of patients, which may have hampered the ability to identify any important associations.

The incremental improvement in both DES and BMS technology was clearly demonstrated in the results of Norwegian Coronary Stent Trial (NORSTENT), where second-generation DESs were not superior to contemporary BMS regarding both major cardiovascular outcomes and post-PCI angina [8]. In our study, DES use at the index PCI was associated with a lower frequency of post-PCI anginal symptoms compared to BMS use. Nevertheless, it is also true that the data regarding the DES/BMS generation used at index PCI were not recorded, so a stratified analysis with stent generation was not possible. Moreover, in our study, DES localisation at the index PCI in small arteries was significantly associated with the Non-RA group. We did not find any data in the literature regarding the association between DES/BMS localisation in small arteries and RA. However, DES has significantly lower rates of repeat revascularisation and major adverse cardiovascular events compared to BMS in the treatment of small coronary arteries [9] and this, perhaps, explains our findings.

Several studies have demonstrated the superiority of DES over BMS regarding the need for target-lesion revascularisation [10-11]. In agreement with previous research, in our study, BMS-ISR was significantly more frequent than DES-ISR, but without significant between-study-group differences. Comparing the DES-ISR subgroup and the BMS-ISR subgroup, only a greater number of native coronary stenoses, suggesting a more massive atherosclerotic load, was associated with BMS-ISR.

Our study has several limitations. First, our study had a small sample size, as previously mentioned; therefore, the statistical power to detect other associations between risk factors for RA may have been reduced. Second, the study was retrospective and included patients from a single centre; thus, our results may not be generalisable.

Conclusions

Advanced age is a risk factor for RA. DES utilisation, especially in the small coronary arteries, appears to be protective against the RA. ISR was associated with RA and occurred more frequently in BMS than in DES. Further studies with a large sample size and longer-term follow-

up are needed to identify other potential risk factors for RA and to determine how to positively influence the evolution of known risk factors.

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