JACOBS PUBLISHERS

OPEN ACCESS

Jacobs Journal of Experimental Cardiology and Research

Research Article

A Multicenter Registry on the Risk-Benefit Balance of Avantgarde Carbofilm-Coated Stent in Real-World Patients at High Risk for Early Discontinuation of Dual Antiplatelet Therapy Undergoing Percutaneous Coronary Intervention: Focus on Diabetic Status

Arturo Giordano MD PhD*, Luigi Sommariva MD, Michele Polimeno MD, Paolo Ferraro MD, Nicola Corcione MD, Stefano Messina MD, Giuseppe Biondi-Zoccai MD, Daniele Pieri MD, Marco Contarini MD, Gennaro Sardella MD

Unità Operativa di Interventistica Cardiovascolare, Presidio Ospedaliero Pineta Grande, Castel Volturno, and Unità Operativa di Emodinamica, Casa di Salute Santa Lucia, San Giuseppe Vesuviano, both in Italy (AG, SM, PF, NC, MP)

Divisione di Cardiologia, Ospedale Belcolle, Viterbo, Italy (LS), Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy (GBZ)

Unità Operattiva di Emodinamica, Ospedale Villa Sofia, Palermo, Italy (DP), Unità Operativa di Emodinamica, Ospedale Umberto I, Siracusa, Italy (MC)

Dipartimento di Scienze Cardiovascolari, Respiratorie, Nefrologiche e Geriatriche, Sapienza Università di Roma, Roma, Italy (GS)

**Corresponding author: Dr. Arturo Giordano, Unità Operativa di Interventistica Cardiovascolare, Presidio Ospedaliero Pineta Grande, Strada Statale Domiziana Km 30, 81030 Castel Volturno CE, Italy, Email: arturogiordano@tin.it*

Funding/Conflicts of Interest: Dr. Giordano has consulted for Medtronic. Dr. Biondi-Zoccai has consulted for Abbott Vascular, Boston Scientific, and Medtronic.

Received: 07-31-2014

Accepted: 08-15-2014

Published: 09-05-2014

Abstract

Objective: We aimed to appraise the risk benefit-balance of the Avantgarde Carbofilm-coated stent in patients undergoing percutaneous coronary intervention (PCI) at high risk of premature dual antiplatelet therapy (DAPT) discontinuation.

Background: Carbofilm coating may increase the biocompatibility of coronary stents, but their risk-benefit balance according to diabetic status remains unclear.

Methods: Patients underwent PCI with the Avantgarde Carbofilm-coated stent and judged by the caring physician at high risk of premature DAPT interruption were retrospectively identified. Subjects were distinguished in 3 groups: non-diabetic (ND), non-insulin-dependent diabetic (NIDDM), and insulin-dependent diabetic (IDDM). Outcomes of interest were major adverse cardiac events (MACE), and their individual components.

Results: A total of 619 patients were included: 490 (79.2%) in the ND group, 95 (15.3%) in the NIDDM group, and 33 (5.3%) IDDM group. After 15±7 months, MACE occurred in 6.9% in the ND group, 17.9% in the NIDDM group, and 21.2% in the IDDM group ($p<0.001$), with similarly trends for death and cardiac death (all $p<0.05$). Multivariable analysis confirmed that those in the ND group were at lower risk than those in the NIDDM group for MACE and death (respectively $p=0.020$ and $p=0.005$).

Conclusion: The Avantgarde Carbofilm-coated stent appears associated with favorable results in patients without diabetes mellitus undergoing PCI and judged at high risk of premature DAPT withdrawal.

Keywords: Acute Coronary Syndrome; Coronary Artery Disease; PTCA; Stent

Introduction

There has been momentous improvements in the medical management of patients with coronary artery disease over the last few decades, but revascularization is still required in unstable patients or those without a satisfactory response to maximal medical therapy [1-2]. Whereas surgical revascularization by means of coronary artery bypass grafting (CABG) appears clearly superior to percutaneous coronary intervention (PCI) in patients with multivessel disease, [3-4] PCI is still beneficial in those with more focal disease or at high risk for surgery.

The ideal device for PCI is still a matter of debate, as bare-metal stents (BMS) are fraught with a predictable risk of restenosis and repeat intervention, [5] and drug-eluting stents (DES) are still considered a potential long-term hazard, especially when DES with permanent polymers with a proven risk of late thrombosis are concerned [6]. Biocompatible coatings aimed at reducing thrombogenicity of metallic endoprosthesis have been proposed, and devices exploiting proprietary Carbofilm coatings have been recently introduced, with favorable preliminary data [7-8]. These devices could prove uniquely useful in those patients at high risk of premature discontinuation of dual antiplatelet therapy (DAPT), which may have ominous implications [9-10]. However, there is uncertainty on their risk-benefit balance, especially in unselected patients, and even more so in patients with diabetes mellitus, which are typically at higher risk of both restenosis and thrombosis [11-13].

We aimed thus to retrospectively appraise the risk-benefit balance of PCI with the Carbofilm-coated Avantgarde stent in real-world patients at high risk of premature DAPT interruption, focusing on diabetic status.

Methods

Design

This was a multicenter retrospective observational study exploiting a prospectively-maintained administrative database for data collection and extraction (Cardioplanet, Esaote, Genoa, Italy). All patients provided written informed consent.

Patients

Patients receiving one or more Avantgarde stent during PCI, or in which implantation of this device was attempted, and who were judged at physician's discretion as being at high risk of premature DAPT discontinuation, were retrospectively retrieved from an explicit query of our administrative database. Indications for PCI with such device, beyond the fact that patients were not deemed suitable for prolonged (>1 month) DAPT, were at operator' discretion. Indeed, all participating centers had previously purchased the Avantgarde stent with the explicit willingness to use it selectively in patients at high risk of premature DAPT discontinuation and this device is typically reserved for patients without high risk of restenosis or those in whom compliance to dual antiplatelet therapy is uncertain. Accordingly, the prototypical subject in whom PCI with Avantgarde is considered is a subject with current or recent unstable coronary artery disease, who is a high risk of bleeding because of his or her specific baseline features, or who is likely to undergo non-cardiac surgery within a few weeks or months (e.g. because of malignancy).

Percutaneous coronary intervention was performed as per standard of care. Thus, intravascular ultrasound (IVUS), optical coherence tomography (OCT) or fractional flow reserve (FFR) were used only when clinically indicated. Similarly, no formal provision was present for pre-dilation or post-dilation, which were also at operators' discretion.

Ancillary medical therapy, including type, intensity, and duration of dual antiplatelet therapy, were also left at the preference of caring physicians. Patients were followed as per routine practice with office visits or phone interviews at 2 weeks, 6 months, 1 year, and 2 years after the index procedure. Specifically, the 2 week time frame was chosen as this was likely the best one to capture in-hospital events or events occurring shortly after discharge, whether 30-day events may have included also events occurring several days or weeks after discharge.

Endpoints and Definitions

The main endpoint of interest for this work was the risk of major adverse cardiac events (MACE), i.e. the composite of death, myocardial infarction, or repeat target vessel revascularization (TVR). Details on individual components of MACE, plus cardiac death, target lesion revascularization (TLR), CABG, and stent thrombosis were also collected.

For the purpose of this work, we distinguished patients without diabetes (non-diabetic [ND]) from thsoe with diabetes, defined as those on oral anti-diabetic medications (non-insulin-dependent diabetic [NIDDM]) or requiring insulin for glycemic control (insulin-dependent diabetic [IDDM]). Indeed, we chose to analyze separately patients with IDDM and NIDDM as they are typically very different in terms of risk of restenosis to bare-metal stents such as the Avantagarde device, as well as in terms of risk of non-target-vessel events.

Statistical Analysis

Continuous variables are reported as mean±standard deviation, and were compared with ANOVA for bivariate analysis.

Categorical variables are reported as n (%), and were compared with chi-squared test for bivariate analysis. Multivariable adjusted analyses were then performed with binary logistic regression, including as covariates all those significantly associated with diabetic status at bivariate analysis, plus all those with an established epidemiologic role on clinical outcomes [14]. Results of multivariable analysis are reported as odds ratio (OR) with 95% confidence interval. Statistical significance was set at the 2-tailed 0.05 level, and p values unadjusted for multiplicity are reported throughout. Computations were performed with SPSS 20 (IBM, Armonk, NY, USA).

Results

A total of 619 patients were included, 490 (79.2%) in the ND group, 95 (15.3%) in the NIDDM group, and 33 (5.3%) IDDM group. Significant differences between these groups were apparent for several baseline variables, including age, prevalence of hypertension, renal failure, prior myocardial infarction, and procedure timing (all p<0.05) (Table 1). Significant differences were found also for several procedural features, including target vessel, stent diameter, and stent length (all p<0.05) (Table 2). In general, patients with diabetes were older, sicker, and had more complex coronary artery lesions.

Table 1. Baseline characteristics

Feature	Non-diabetic (N=490)	Non-insulin-dependent diabetic (N=95)	Insulin-dependent diabetic (N=33)	Total (N=619)	P
Age (years)	66.1±11.8	69.4±10.1	72.7±9.2	66.9±9.2	<0.001
Female gender	108 (22.0%)	21 (22.1%)	13 (39.4%)	142 (22.9%)	0.070
Height (cm)	168.3±7.9	169.9±9.1	167.6±7.0	168.4±8.0	0.647
Weight (kg)	76.6±13.3	81.5±12.3	77.8±9.4	77.1±13.1	0.222
Hypertension	251 (51.1%)	67 (70.5%)	23 (69.7%)	341 (55.1%)	0.001
Dyslipidemia	68 (13.8%)	11 (11.6%)	3 (9.1%)	82 (13.2%)	0.644
Current smoking	96 (19.6%)	17 (17.9%)	4 (12.1%)	117 (18.9%)	0.552
Renal failure	23 (4.7%)	8 (8.4%)	12 (36.4%)	43 (6.9%)	<0.001
Prior AMI	39 (7.9%)	11 (11.6%)	8 (24.2%)	58 (9.4%)	0.006
Prior PCI	51 (10.4%)	13 (13.7%)	5 (15.2%)	69 (11.1%)	0.487
Timing of procedure					0.031
Elective	363 (73.9%)	83 (87.4%)	29 (87.9%)	475 (76.7%)	
Urgent	79 (16.1%)	8 (8.4%)	2 (6.1%)	89 (14.4%)	
Emergent	49 (10.0%)	4 (4.2%)	2 (6.1%)	55 (8.9%)	

AMI=acute myocardial infarction; PCI=percutaneous coronary intervention

Table 2. Procedural features

Feature	Non-diabetic (N=490)	Non-insulin-dependent diabetic (N=95)	Insulin-dependent diabetic (N=33)	Total (N=619)	P
Target vessel					0.009
Left main	6 (1.2%)	1 (1.0%)	3 (8.3%)	10 (1.5%)	
Left anterior descending	198 (38.3%)	36 (36.0%)	13 (36.1%)	247 (37.8%)	
Left circumflex	141 (27.3%)	24 (24.0%)	9 (25.0%)	174 (26.6%)	
Right coronary artery	170 (32.9%)	36 (36.0%)	10 (27.8%)	216 (33.1%)	
Saphenous vein graft	2 (0.4%)	3 (3.0%)	1 (2.8%)	6 (0.9%)	
Lesion type					0.477
Ellis A	76 (14.7%)	15 (15.0%)	4 (11.1%)	95 (14.5%)	
Ellis B1	186 (36.0%)	32 (32.0%)	12 (33.3%)	230 (35.2%)	
Ellis B2	167 (32.3%)	36 (36.0%)	11 (30.6%)	214 (32.8%)	
Ellis C	65 (12.6%)	13 (13.0%)	7 (19.4%)	85 (13.0%)	
Restenosis	5 (1.0%)	2 (2.0%)	2 (5.6%)	9 (1.4%)	
Thrombosis	18 (3.5%)	2 (2.0%)	0	20 (3.1%)	
Baseline diameter stenosis (%)	87.5±10.7	85.7±9.6	84.6±10.4	87.0±10.5	0.113
Lesion length (mm)	14.4±8.1	15.9±12.0	16.2±8.4	14.7±8.8	0.191
Bifurcation lesion	25 (4.8%)	5 (5.0%)	1 (2.8%)	31 (4.7%)	0.847
Calcified lesion	93 (18.0%)	20 (20.0%)	5 (13.9%)	118 (18.1%)	0.712
Stent diameter (mm)	3.12±0.69	2.97±0.78	3.17±0.77	3.09±0.72	0.003
Stent length (mm)	15.5±5.5	14.8±5.6	16.8±5.0	15.5±5.5	0.004
Procedure duration (minutes)	70.7±29.7	65.8±35.7	66.9±18.0	69.9±30.1	0.554
Procedural success	490 (94.8%)	98 (98.0%)	35 (97.2%)	623 (95.4%)	0.321

Significant differences in clinical outcomes were apparent already at 2 weeks at bivariate unadjusted analysis (Table 3). Specifically, patients without diabetes were at lower short-term risk of MACE, death, and cardiac death (all p<0.05). Similarly significant differences in favor of the ND group were evident at long-term (14.6±6.9 months) follow-up, with a lower risk of MACE, death, and cardiac death. Conversely, the rate of myocardial infarction, TLR, TVR, CABG or stent thrombosis was homogeneously low despite the ubiquitous high risk for premature DAPT discontinuation, and not significantly different in the groups. Notably, all cardiac deaths ischemic in etiology (either sudden or due to myocardial infarction).

Table 3. Clinical results at short- and long-term.

Feature	Non-diabetic (N=490)	Non-insulin-dependent diabetic (N=95)	Insulin-dependent diabetic (N=33)	Total (N=619)	P
Two-week follow-up					
MACE	13 (2.7%)	8 (8.4%)	4 (12.1%)	25 (4.0%)	0.002
Death	8 (1.6%)	8 (8.4%)	3 (9.1%)	19 (3.1%)	<0.001
Cardiac death	0	4 (4.2%)	1 (3.0%)	5 (0.8%)	<0.001
AMI	3 (0.6%)	0	0	3 (0.5%)	0.675
TLR	1 (0.2%)	0	0	1 (0.2%)	0.676
TVR	3 (0.6%)	0	1 (3.0%)	4 (0.6%)	0.169
CABG	2 (0.4%)	0	0	2 (0.3%)	0.770
Stent thrombosis	1 (0.2%)	0	0	1 (0.2%)	0.877
Long-term follow-up					
Follow-up duration	14.1±6.6	16.2±7.6	17.4±7.2	14.6±6.9	0.003
MACE	34 (6.9%)	17 (17.9%)	7 (21.2%)	58 (9.4%)	<0.001
Death	9 (1.8%)	8 (8.4%)	3 (9.1%)	20 (3.2%)	0.001
Cardiac death	0	4 (4.2%)	1 (3.0%)	5 (0.8%)	<0.001
AMI	3 (0.6%)	0	0	3 (0.5%)	0.675
TLR	22 (4.5%)	8 (8.4%)	4 (12.1%)	34 (5.5%)	0.070
TVR	24 (4.9%)	9 (9.5%)	4 (12.1%)	37 (6.0%)	0.070
CABG	2 (0.4%)	1 (1.1%)	0	3 (0.5%)	0.651
Stent thrombosis	1 (0.2%)	0	0	1 (0.2%)	0.878

AMI=acute myocardial infarction; CABG=coronary artery bypass grafting; MACE=major adverse cardiac events; TLR=target lesion revascularization; TVR=target vessel revascularization

Multivariable analysis confirmed that patients in the ND group were still at lower long-term risk of MACE and death even when adjusting for potential confounders (Table 4). Conversely, the differences between the IDDM and ND groups were no longer significant after adjustment, suggesting that most of the risk associated with diabetes might lie in the NIDDM group.

Table 4. Unadjusted and multivariable-adjusted clinical results at long-term

Feature	Non-insulin-dependent diabetic vs non-diabetic	Insulin-dependent diabetic vs non-diabetic	Insulin-dependent diabetic vs non-insulin-dependent diabetic
Unadjusted results			
MACE	OR=2.93 (1.56-5.50), p=0.001	OR=1.90 (1.21-2.99), p=0.005	OR=1.24 (0.46-3.31), p=0.674
Death	OR=4.93 (1.85-13.11), p=0.001	OR=2.31 (1.17-4.56), p=0.015	OR=1.09 (0.27-4.37), p=0.906
TVR	OR=2.04 (0.92-4.53), p=0.081	OR=1.64 (0.93-2.87), p=0.085	OR=1.32 (0.38-4.60), p=0.665
Multivariable-adjusted results*			
MACE	OR=2.40 (1.15-5.03), p=0.020	OR=1.66 (0.94-2.92), p=0.079	OR=1.34 (0.34-5.51), p=0.653
Death	OR=7.22 (1.81-28.86), p=0.005	OR=1.73 (0.73-4.07), p=0.214	OR=0.76 (0.09-6.84), p=0.807
TVR	OR=1.70 (0.66-4.33), p=0.272	OR=1.71 (0.84-3.45), p=0.137	OR=2.03 (0.27-15.50), p=0.495

*reported as odds ratio (OR) with 95% confidence intervals, and simultaneously adjusting for age, gender, hypertension, dyslipidemia, smoking status, renal failure, prior AMI, prior PCI, elective procedure, left main revascularization, baseline diameter stenosis, lesion length, calcified lesion, Ellis C lesion, bifurcation lesion, stent diameter, stent length, and procedural success; MACE=major adverse cardiac events; PCI=percutaneous coronary intervention; TVR=target vessel revascularization.

Discussion

This study, the largest reporting to date on the use of the Carbofilm-coated Avantgarde stent in unselected patients undergoing PCI, suggests that this device appears associated with favorable results in patients without diabetes mellitus undergoing PCI. These findings appear even more insightful given that the Avantgarde was used selectively in patients at high risk of premature DAPT discontinuation.

The management of coronary artery disease has improved substantially in recent years, thanks to developments in medical therapy and revascularization strategy. More poignantly, devices for percutaneous coronary intervention have changed substantially, and the interventionist's armamentarium now includes drug-eluting stents with bioresorbable polymers, bioresorbable vascular scaffolds, and drug-coated balloons [15-17]. Nonetheless, bare metal stents still represent a useful tool especially in patients unsuitable for long-term DAPT and/or at low risk of restenosis (e.g. because of focal lesions in large vessels). In addition, specific coatings can be added to bare metal stents to improve their biocompatibility, foster endothelialization, and reduce thrombogenicity. Carbofilm coating is a typical example of such coatings, as it aims at improving both short-term safety and long-term efficacy of bare metal stents.

Preliminary data on the Carbofilm-coated Avantgarde stent have already been reported, and include a pilot clinical experience [7], as well as a mechanistic study exploiting early optical coherence tomography to appraise strut coverage [8].

Briguori et al used the Avantgarde in 42 patients with undeferrable non-cardiac surgery (actually performed an average of 27 days after PCI) [7] Only one patient had a MACE, precisely 12 days after PCI and 3 days after vascular surgery for abdominal aortic aneurysm. Prati et al showed in 20 patients with STEMI and multivessel disease, that strut coverage 4-7 days after Avantgarde implantation in the culprit lesion was satisfactory, with only 3.9% uncovered struts, 8.0% malapposed struts, and 2.6% thrombus-laden struts [8]. These data suggest that the Avantgarde provides satisfactory results even in patients requiring early DAPT discontinuation or with high-risk lesions with substantial thrombus burden.

Our present findings confirm these preliminary observations in much smaller studies. Specifically, we found that Avantgarde was associated with favorable results in non-diabetic patients. Results in diabetics were inferior to those without this condition, but this in keeping with prior evidence on the unfavorable short- and long-term prognosis faced by such patients when undergoing PCI, given their more diffuse atherosclerotic burden and higher risk for thrombotic complications [18-20]. The overall evidence suggests that insulin-dependent diabetics are even at higher risk of adverse events than non-insulin-dependent diabetics, as they may represent a subgroup of diabetics with poorly controlled glycemia and persisting insulin resistant despite optimal oral medication regimens [21,22]. Reports calling into question this paradigm are however available, and testify that improvements in management strategies may finally equalize the prognosis of diabetics and non-diabetics [23-24].

An important consideration to bear in mind when analyzing our results is that all patients included in our retrospective registry were deemed, at the physician's discretion, at high risk of premature DAPT discontinuation. Accordingly, all subjects were at heightened risk of thrombotic complications. In light of these specific clinical features, the fact that only 1 stent thrombosis was adjudicated supports the hypothesis that the Carbofilm coated Avantgarde has low thrombogenicity, and may thus be safely used in such patients. The fact that diabetics had a more unfavorable prognosis than non-diabetics suggests conversely that additional efforts to improve the outcome of these patient should be pursued. These may include more potent antithrombotic therapy [25], optimization of stenting techniques with intravascular imaging [8] or reliance on other revascularization strategies (i.e. coronary artery bypass surgery) [3].

This work has several drawbacks, including those of retrospective observational studies including unselected real-world patients and the lack of an explicit set of inclusion and exclusion criteria such as those typical of prospective studies. Specifically, the risk of confounding due to selection, performance, and attrition and adjudication bias cannot be ruled out. Indeed, stent choice, as well as all other management decisions, was at physicians' discretion. Accordingly, we cannot rule out that the Avantgarde stent was used selectively in very high risk diabetics in comparison to very low risk non-diabetics, with such high risk features only partially adjustable for. Thus, these results should best be viewed as hypothesis-generating, and require formal prospective testing in a pragmatic randomized clinical trial comparing patients undergoing PCI with Avantgarde versus subjects undergoing PCI with new-generation DES,(15) or bioresorbable devices [16]. In addition, details on type and duration of DAPT were not collected systematically and thus no formal analysis of their impact on clinical outcomes (such as MACE) could be performed in the present work. Notwithstanding these limitations, the prevalence and burden of coronary artery disease in patients with or without diabetes, and the common need for minimally invasive coronary revascularization despite the frequent occurrence of high risk features for premature dual antiplatelet therapy discontinuation mean that work may be informative to the large audience of cardiovascular specialists.

In conclusion, the Avantgarde Carbofilm-coated stent appears associated with favorable results in patients without diabetes mellitus undergoing PCI despite being deemed at high risk of premature DAPT.

References

1. Boden W E, O'Rourke R A, Teo K K, Hartigan P M, Maron D J et al. Optimal medical therapy with or without PCI for stable coronary disease. N Engl J Med. 2007, 356: 1503-1516.

2. De Bruyne B, Pijls N H, Kalesan B, Barbato E, Tonino P A et al. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. N Engl J Med. 2012, 367: 991-1001.

3. Farkouh M E, Domanski M, Sleeper L A, Siami F S, Dangas G et al. Strategies for multivessel revascularization in patients with diabetes. N Engl J Med. 2012, 367: 2375-2384.

4. Mohr F W, Morice M C, Kappetein A P, Feldman T E, Ståhle E et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. Lancet. 2013, 381: 629-638.

5. Biondi-Zoccai G G, Agostoni P, Abbate A, Testa L, Burzotta F et al. Adjusted indirect comparison of intracoronary drug-eluting stents: evidence from a metaanalysis of randomized bare-metal-stent-controlled trials. Int J Cardiol. 2005, 100: 119-123.

6. Palmerini T, Biondi-Zoccai G, Della Riva D, Stettler C, Sangiorgi D, D'Ascenzo F et al. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. Lancet. 2012, 379: 1393-1402.

7. Briguori B, Visconti G, De Micco F, Focaccio A. The Avantgarde Carbostent in Patients Scheduled for Undelayable Non-cardiac Surgery. Thrombosis. 2012, 2012: 372371.

8. Prati F, Monaco S, Pawlosky T, Mallus MT, Di Giorgio A et al. Early vessel healing of the Avantgarde cobalt-chromium coronary stent: the ON-GARDE OCT study. J Cardiovasc Med (Hagerstown). 2013, 14: 276-280.

9. Biondi-Zoccai GG, Lotrionte M, Agostoni P, Abbate A, Fusaro M et al. A systematic review and meta-analysis on the hazards of discontinuing or not adhering to aspirin among 50,279 patients at risk for coronary artery disease. Eur Heart J. 2006, 27: 2667-2674.

10. Mehran R, Baber U, Steg PG, Ariti C, Weisz G et al. Cessation of dual antiplatelet treatment and cardiac events after percutaneous coronary intervention (PARIS): 2 year results from a prospective observational study. Lancet. 2013, 382: 1714-1722.

11. Cosgrave J, Melzi G, Biondi-Zoccai GG, Airoldi F, Chieffo A et al. Drug-eluting stent restenosis the pattern predicts the outcome. J Am Coll Cardiol. 2006, 47: 2399-2404.

12. Sheiban I, Garrone P, Sillano D, Biondi-Zoccai G, Sciuto F, Omedè P et al. Impact of diabetes mellitus on early and long-term results of percutaneous drug-eluting stent implantation for unprotected left main coronary disease. J Cardiovasc Med (Hagerstown). 2008, 9: 1246-1253.

13. D'Ascenzo F, Bollati M, Clementi F, Castagno D, Lagerqvist B et al. Incidence and predictors of coronary stent thrombosis: evidence from an international collaborative meta-analysis including 30 studies, 221,066 patients, and 4276 thromboses. Int J Cardiol. 2013, 167: 575-584.

14. Biondi-Zoccai G, Romagnoli E, Agostoni P, Capodanno D, Castagno D et al. Are propensity scores really superior to standard multivariable analysis? Contemp Clin Trials. 2011, 32: 731-740.

15. Palmerini T, Biondi-Zoccai G, Della Riva D, Mariani A, Sabaté M et al. Clinical outcomes with bioabsorbable polymer- versus durable polymer-based drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. J Am Coll Cardiol. 2014, 63: 299-307.

16. Serruys PW, Ormiston JA, Onuma Y, Regar E, Gonzalo N et al. A bioabsorbable everolimus-eluting coronary stent system (ABSORB): 2-year outcomes and results from multiple imaging methods. Lancet. 2009, 373: 897-910.

17. Unverdorben M, Vallbracht C, Cremers B, Heuer H, Hengstenberg C, Maikowski C et al. Paclitaxel-coated balloon catheter versus paclitaxel-coated stent for the treatment of coronary in-stent restenosis. Circulation. 2009, 119: 2986-2994.

18. Jensen LO, Thayssen P, Junker A, Maeng M, Tilsted HH, Kaltoft A et al. Comparison of outcomes in patients with versus without diabetes mellitus after revascularization with everolimus- and sirolimus-eluting stents (from the SORT OUT IV trial). Am J Cardiol. 2012, 110: 1585-1591.

19. Banning AP, Westaby S, Morice MC, Kappetein AP, Mohr FW et al. Diabetic and nondiabetic patients with left main and/or 3-vessel coronary artery disease: comparison of outcomes with cardiac surgery and paclitaxel-eluting stents. J Am Coll Cardiol. 2010, 55: 1067-1075.

20. Daemen J, Kuck KH, Macaya C, LeGrand V, Vrolix M et al. Multivessel coronary revascularization in patients with and without diabetes mellitus: 3-year follow-up of the ARTS-II (Arterial Revascularization Therapies Study-Part II) trial. J Am Coll Cardiol. 2008, 52: 1957-1967.

21. Silber S, Serruys PW, Leon MB, Meredith IT, Windecker S

et al. Clinical outcome of patients with and without diabetes mellitus after percutaneous coronary intervention with the resolute zotarolimus-eluting stent: 2-year results from the prospectively pooled analysis of the international global RESOLUTE program. JACC Cardiovasc Interv. 2013, 6: 357-368.

22. Biondi-Zoccai GG, Abbate A, Liuzzo G, Biasucci LM. Atherothrombosis, inflammation, and diabetes. J Am Coll Cardiol. 2003, 41: 1071-1077.

23. Sheiban I, Garrone P, Sillano D, Biondi-Zoccai G, Sciuto F et al. Impact of diabetes mellitus on early and long-term results of percutaneous drug-eluting stent implantation for unprotected left main coronary disease. J Cardiovasc Med (Hagerstown). 2008, 9: 1246-1253.

24. Kirtane AJ, Patel R, O'Shaughnessy C, Overlie P, McLaurin B et al. Clinical and angiographic outcomes in diabetics from the ENDEAVOR IV trial: randomized comparison of zotarolimus- and paclitaxel-eluting stents in patients with coronary artery disease. JACC Cardiovasc Interv. 2009, 2: 967-976.

25. Biondi-Zoccai G, Lotrionte M, Agostoni P, Abbate A, Romagnoli E et al. Adjusted indirect comparison meta-analysis of prasugrel versus ticagrelor for patients with acute coronary syndromes. Int J Cardiol. 2011, 150: 325-331.