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Management of distal/bifurcation left main restenosis after drug eluting stents implantation: Single center experience

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ABSTRACT

Objectives: Restenosis after drug eluting stent (DES) implantation in the distal/bifurcation left main (DBLM) remains challenging to manage. The aim of this study was to assess the in-stent restenosis (ISR) after DES implantation in DLM and to evaluate current management strategy.
Methods: The medical records of patients referred for LM distal/bifurcation percutaneous coronary interventions (PCI) from the same Cardiology Unit in the January 2007 to December 2012 period were reviewed for PCI technique, stent type, restenosis type, restenosis treatment and management (CABG, balloon angioplasty only, alternative DES implant, drug eluting balloon angioplasty).
Results: Fourteen patients (5 females, mean age 75.1 ± 8.3 years) out of 89 (15.7%) having undergone a percutaneous coronary interventions on DBLM with DES, developed restenosis (everolimus stents in 10 patients, zotarolimus stents in 4 patients). Technique used at the first implant included stenting of the main branch in 4 patients, culottes stenting in 6 patients and T-stent in 4 patients. The mean time elapsed from the first angioplasty and ISR intervention was 7.6 ± 3.6 months. Restenosis treatments included: implantation of a different DES (in 3 patients), implantation of a bare-metal stent (in 2 patients), simple balloon angioplasty (in 4 patients), and drug-eluting balloon (5 patients). At 6-month angiographic control second restenosis rate was 14.2%. After a mean follow-up of 38.5 ± 24.4 months the target vessel revascularization was 14.3%: surgery was the final choice in two patients due to recurrent restenosis. Incidence of major adverse cardiac event was 28.5%.
Conclusions: The occurrence of restenosis after DBLM following DES implantation is not frequent but remains difficult to manage. In our small anecdotal series, all the different strategies including implantation of different DES, balloon angioplasty, bare-metal stent implantation and drug-eluting balloon angioplasty appeared equally effective in maintaining arterial patency.

1. Introduction

Current guidelines discourage percutaneous interventions of left main (LM), in particular distal/bifurcation left main because of increase in mortality and target vessel revascularization (TVR) in such patients compared to surgical bypass grafting [1]. Nevertheless, patients noncandidates for surgery due to age or comorbidities are currently submitted to LM interventions as the unique revascularization option. In several studies drug eluting stent (DES) implantation in left main (LM) appeared to be safe and effective, at least at mid-term [2–6]. However in-stent restenosis (ISR) after DES in LM disease is still occurring with an incidence of 14%–19%. Limited data exist on occurrence of distal/bifurcation left main (DBLM) ISR after DES and optimal management strategy is still debated. Our retrospective study is aimed to evaluate the incidence of DBLM restenosis after DES implantation in patients not candidates for surgery and to suggest a management strategy.

2. Methods

The medical records of patients referred for DBLM percutaneous coronary interventions (PCI) in the January 2007 to December 2012 period were reviewed. Patient medical history and procedural data were reviewed, recording clinical (cardiovascular risk factors, Canadian Cardiovascular Score class, EUROSCORE [7]) and angiographic characteristics (lesion/s location and severity. SYNTAX score [8], MEDINA classification [9]), as well as the equipment and techniques used at the time of PCI including stent type and size, restenosis type, restenosis treatment and management (CABG, balloon angioplasty only, alternative DES implant, drug eluting

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balloon angioplasty). Per our institutional protocol, follow-up was conducted by physical examination at 1, 6, 12 months and yearly whereas angiographic control was scheduled at 6–8 months. Induced ischemia test by means of nuclear stress test or stress echocardiography was scheduled yearly.

2.1. Protocol and definitions

All interventions were performed according to current standard guidelines, and the final interventional strategy, including the use of glycoprotein IIb/IIIa inhibitors, was left entirely to the discretion of the operator. Angiographic success was defined as residual stenosis 30% by visual analysis in the presence of Thrombolysis in Myocardial Infarction (TIMI) 3 flow grade. All patients were advised to maintain the use of aspirin lifelong. Twelve-month clopidogrel treatment (75 mg/d) was recommended for patients treated.

2.2. End Point Definitions and Clinical Follow-Up

Re-angiogram at 6–8 months (±30 days) after the index stenting procedure was scheduled for all patients unless clinically indicated earlier. Quantitative coronary angiographic (QCA) analysis at baseline, post-stenting and follow-up was performed using edge detection techniques (CAAS II 5.0 version; Pie Medical, Maastricht, Netherlands). Binary restenosis was defined as stenosis ≥50% of the luminal diameter in target lesions.

Angiographic measurements included the stented segment as well as the margins 5-mm proximal and distal to the stent. Major adverse cardiac events were defined as (1) death, (2) nonfatal myocardial infarction (MI), or (3) target vessel revascularization (TVR). All deaths were considered to be of cardiac origin unless a noncardiac origin was established clinically or at autopsy. AMI was diagnosed by a rise following Thygesen K et al. [10]. TVR was defined as a repeated intervention (surgical or percutaneous) to treat a luminal stenosis within the stent or in the 5-mm distal or proximal segments adjacent to the stent, including the ostium of the left anterior descending artery (LAD) and/or circumflex artery. Stent thrombosis was classified according to the Academic Research Consortium (ARC) definitions as definite, probable or possible, as early (0–30 days), late (31–360 days) or very late (>360 days).

In-stent restenosis (ISR) was classified as focal (<10 mm long), diffuse (>10 mm long), proliferative (>10 mm long and extending outside the stent edges), or totally occluded [11].

Information about in-hospital outcomes was obtained from an electronic clinical database for patients maintained at our institution and by review of hospital records for those discharged to referring hospitals. Post-discharge survival status was obtained from the Municipal Civil Registries. Information on occurrence of AMI or repeated interventions at follow-up was collected by consulting our institutional electronic database and by contacting referring physicians and institutions and all living patients.

2.3. Statistical analysis

Continuous variables are described as mean ± standard deviation, and categorical variables are described as proportions. Stepwise logistic regression analysis was used to determine independent determinants of ISR. The analysed variables were age >65, sex, SYNTAX score >20, presentation at first interventions (ST-elevation ACS, non-ST elevation ACS, effort angina, cardiogenic shock), total implanted stent length, number of implanted stent, used technique (T-stenting, culottes stenting, main branch only). Statistical analysis was performed using a statistical software package (SAS for Windows, version 8.2; SAS Institute; Cary, NC). A probability value of < 0.05 was considered to be statistically significant.

3. Results

Fourteen patients (5 females, mean age 75.1 ± 8.3 years, Table 1) out of 89 (15.7%) judged not candidates for surgery previously submitted to PCI on distal/bifurcation left main with DES, developed restenosis at the site of previous stents implantation (Table 1, Table **2**): compared with non ISR patients, patients who developed restenosis had an higher risk profile and more frequently complex lesion and longer stents and were more frequently treated with T-stent technique at the time of first DES implantation.

Stents involved were Resolute Endeavour (Medtronic Ireland, Galway, Ireland) in 6 patients, Resolute Integrity (Medtronic Ireland, Galway, Ireland) in 2 patients and Promus (Boston Scientific, Natick, MA, USA) in the rest of 6 patients.

Technique used at the first implant included stenting of the main branch in 4 patients, culottes stenting in 3 patients and T-stent in 7 patients. The mean time elapsed from the first angioplasty and restenosis intervention was 7.6 ± 3.6 months. The QCA mean LM diameter was 2.8 ± 1.3 mm compared to 3.4 ± 1.5 mm of patients with no restenosis ($p < 0.01$).

On logistic regression analysis independent predictors of ISR were first clinical presentation of cardiogenic shock (OR 3.0, 1.5–4 [95% CI], $p < 0.01$), Syntax score >20 (OR 3.3, 1.2–3.8 [95% CI], $p < 0.01$) and total stent length per patients >25 mm (OR 3.1, 2.0–5.3 [95% CI], $p < 0.01$), T-stenting(OR 1.8, 1.0–3.2 [95% CI], $p < 0.01$).

All 14 patients underwent IVUS guided procedure: on the basis of IVUS, ISR lesions were focal in 3 patients (21.4%), diffuse in 6 patients (42.8%) and proliferative in 5 patients (35.7%). Malposition of the previous stent was diagnosed in 5 patients (35.7%, Fig. 1).

Restenosis treatments included: implant of a different DES (Resolute Integrity in 5 patients), simple balloon angioplasty (in 4 patients), and drug-eluting balloon (5 patients). At 6-month angiographic control second restenosis rate was 14.2%.

At a mean follow-up of 38.5 ± 24.4 months, TVR was 14.3%: mini-invasive surgery was the final choice in two patients due to recurrent restenosis after second treatment whereas other two patients underwent carbofilm bare metal stent implantation on LM-LAD (AvantGard, CID spa, Saluggia, Italy) and simple POBA on LCx for patients' inability to assume double antiaggregation for the long term. Incidence of major adverse cardiac event was 28.5% (Table 3).

Table 1
Demographical and clinical data.

	DLM ISR No. 14	DLM no ISR No. 75	p
Risk Factors (%)			
Hypertension	13 (92.8)	54 (72.0)	<0.01
Hypercholesterolemia	12 (85.7)	60 (80)	ns
Diabetes	13 (92.8)	47 (62.6)	<0.01
Smoking	10 (71.4)	52 (69.3)	ns
Valvular heart disease	9 (64.2)	48 (64.0)	ns
EF (%) (±SD)	39 ± 10.3	51 ± 12.6	<0.03
CCS class (±SD)	3.5 ± 0.5	2.4 ± 0.7	<0.03
Medical history, %			
PCI	4 (28.6)	20 (26.7)	ns
AMI	6 (42.8)	23 (30.6)	<0.03
Transient ischemic attack/stroke	2 (14.3)	10 (13.3)	ns
Heart failure	1 (7.2)	3 (4)	ns
Severe COPD	6 (42.8)	20 (26.7)	ns
Peripheral arterial disease	7 (50)	23 (30.6)	<0.03
Carotid artery disease	3 (21.6)	22 (29.3)	ns
Clinical presentation (%)			
Effort angina	2 (14.4)	40 (53.3)	<0.01
Non-ST elevation ACS	4 (28.4)	20 (26.7)	Ns
ST-elevation ACS	8 (56.8)	15 (20.0)	<0.01
Cardiogenic shock at entry	3 (21.6)	1 (1.3)	ns

AMI = acute myocardial infarction; ACS = acute coronary syndrome; CCS = Canadian Cardiovascular Score; EF = ejection fraction calculated from left ventricle angiography; TIA = transient ischemic attack; SD = standard deviation.