

Prevalence of Drug Eluting Stent Restenosis and Its Correlation with Culprit Coronary Artery

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Abstract: In-Stent Restenosis (ISR) remains a significant problem for the treatment of coronary artery disease (CAD). Our study was conducted to evaluate the prevalence of significant restenosis of drug eluting stent (DES), as to its correlation with the culprit coronary artery. A retrospective study was conducted on 924 consecutive patients undergoing percutaneous coronary intervention (PCI) for DES implantation and who were followed-up by cardiac coronarography within 1 year. Cardiac coronarography films were reviewed for the presence or the absence of significant ISR, and for detection of the underlying culprit coronary artery. 2x2 tables and Chi square test were used. P value<0.05 was considered significant. The revision of cardiac coronarography films of follow-up for 924 included angioplasties showed significant ISR in 165 DES out of the 1494 implanted ones. Statistical analysis estimates the prevalence of DES restenosis at 11%. Taking into consideration the different coronary arteries, it is respectively: 8.79% in Left Anterior Descending (LAD) where ISR was found in 63 stents out of the 654 inserted ones, 11.38% in circumflex (Cx) where ISR was found in 42 stents out of the 327 inserted ones, and 14.7% in right coronary artery (RCA) where ISR was found in 60 stents out of the 342 implanted ones. A negative significant relationship was detected between the prevalence of ISR and LAD coronary artery lesion in opposition to a positive significant relationship between the prevalence of ISR and RCA lesion. The prevalence of significant ISR of DES is 11% and it is significantly higher in stents implanted in RCA as compared to stents implanted in Cx and LAD with statistical evidence of significant correlation between the prevalence of ISR and the involved culprit coronary artery.

Keywords: In-Stent Restenosis, Drug Eluting Stent, Coronary Artery Disease, Percutaneous Intervention

1. Introduction

Cardiovascular disease including coronary artery disease (CAD), valvular heart disease and heart failure are the leading cause of death worldwide. It is still responsible approximately for one third of the death in population aged above 35 years [1]. In parallel, the modalities of treatment were developed rapidly in particular with the era of percutaneous coronary intervention and the generation of drug eluting stent, most commonly used modality in the treatment of patients with CAD, specially acute coronary syndrome [2]. Even though, PCI and DES generation were associated with a decrease in mortality, but In-stent restenosis (ISR) remains a significant limitation for CAD treatment. DES was associated with a higher incidence of late ISR. This study was conducted to

evaluate the prevalence of significant ISR of DES and its correlation with the culprit coronary artery.

2. Materials and Methods

A retrospective study was conducted on 924 consecutive patients who were referred for PCI and DES insertion in the cardiovascular department of Notre-Dame de Secours University Hospital (NDS-UH) between December 2014 and December 2017, and who were followed-up with cardiac coronarography within 1 year. Patients not followed-up by cardiac coronarography within 1 year after the primary PCI when DES was inserted and patients in whom Bare Metallic

Stent (BMS) was inserted were excluded from this study. Patients known to have coronary artery bypass graft were excluded. Cardiac coronarography within one year of the primary angioplasty was indicated due to presence of symptoms related to CAD like chest pain, shortness of breath, angina... Cardiac coronarography films of follow-up were reviewed for the presence or the absence of significant ISR, and for the detection of the culprit coronary artery. Coronary angiography films were reviewed by the same reference doctors in the cardiovascular department of NDS-UH. A stent luminal narrowing $\geq 50\%$ was considered significant. This study was approved by the ethics committee of NDS-UH and written consent was obtained from the hospital to allow data collection. A p value less than 0.05 was considered significant. 2x2 tables and SPSS version 19.0 were used.

3. Results

This study includes 924 patients with mean age of 57 ± 10 years. Table 1 shows patients demographic data.

Table 1. Patients demographic data (2010).

Variable	N (%)
Gender	
Male	645 (69.8%)
Female	279 (30.2%)
Diabetic patient	438 (47.4%)
Hypertensive patient	443 (48%)
Mean Age	57 ± 10 years

The revision of films of cardiac coronarography done within 1 year for follow-up of the 924 included PCI with DES insertion reveals the presence of significant ISR in 165 stents (11%) among the 1494 implanted stents. Of 1494 inserted DES, 717 stents (48%) were inserted in Left anterior Descending (LAD) artery from which 654 (91.21%) were patent and 63 stents (8.79%) had ISR, 369 stents (24.7%) were inserted in circumflex (Cx) artery from which 327 (88.62%) were patent and 42 (11.38%) had ISR, and 408 (27.3%) were inserted in right coronary artery (RCA) from which 348 (85.29%) were patent and 60 (14.71%) had ISR (Figures 1-2) (Table 2).

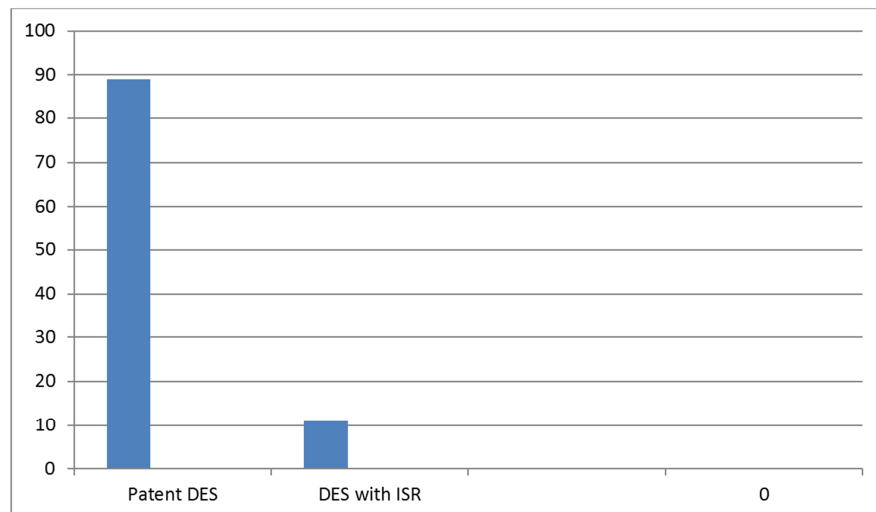


Figure 1. Overall prevalence of ISR of DES.

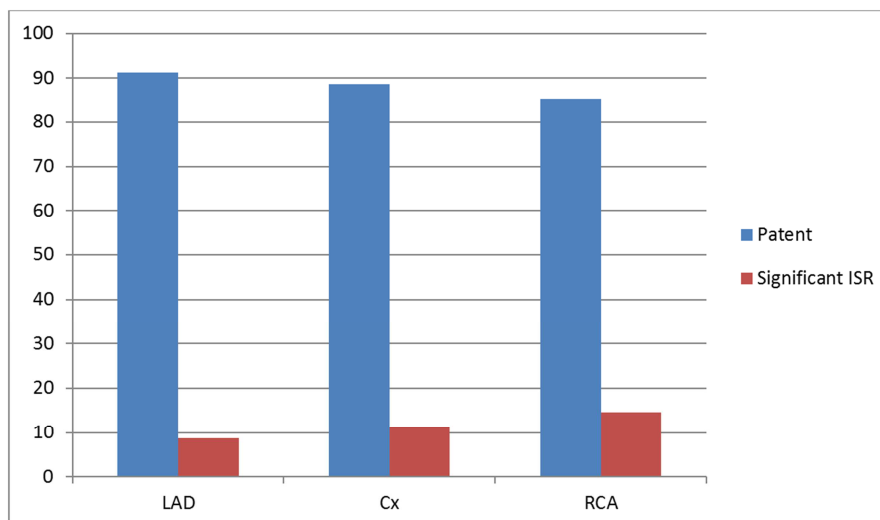


Figure 2. Prevalence of ISR of DES related to coronary arteries.

Table 2. Results summary.

	Patent	Restenosis	Total
LAD	654(91.21%)	63 (8.79%)	717 (48%)
Cx	327(88.62%)	42(11.38%)	369(24.7%)
RCA	348 (85.3%)	60(14.7%)	408(27.3%)
Total	1329 (89%)	165 (11%)	1494

Statistical analysis evaluates the prevalence of DES restenosis at 11% and respectively according to different coronary arteries: 8.79% in LAD, 11.38% in Cx, and 14.7% in RCA. Statistical analysis shows a significant negative correlation between a lesion treated by stent insertion on LAD and the prevalence of ISR with a p value of 0.0079 (Table3), in opposition to a significant positive relationship between a lesion treated by stent insertion on RCA and the prevalence of ISR with a p value of 0.006 (Table 5), and notes the absence of significant correlation between a lesion treated by stent insertion on Cx and the prevalence of ISR (p=0.8114) (Table 4).

Table 3. Relationship between LAD lesion and ISR.

	ISR	Patent	Total
LAD	63	654	717
Other coronaries	102	675	777
Total	165	1329	1494

O.R= 0.6375 C.I {0.46-0.89} P=0.0079

Table 4. Correlation between Cx lesion and ISR.

	ISR	Patent	Total
Cx	42	327	369
Other coronaries	123	1002	1125
Total	165	1329	1494

O.R=1.0463 C.I{ 0.72-1.52} P=0.8114

Table 5. Correlation between RCA lesion and ISR.

	ISR	Patent	Total
RCA lesion	60	348	408
Other coronary lesion	105	981	1086
Total	165	1329	1494

O.R=1.61 C.I{1.61-2.26} P=0.006

4. Discussion

Percutaneous coronary intervention (PCI) technology has revolutionized the field of cardiology but ISR that is a complex disease with multiple pathophysiological mechanisms and various risk factors that remain the major limitation of PCI and angioplasty [4-5]. The generation of DES has dramatically reduced the rate of ISR and subsequent target lesion revascularization compared with BMS but it is associated with relevant issues such as late stent thrombosis and late restenosis [6]. Different mechanisms of ISR were identified like early elastic return (recoil), vascular remodeling, and neointimal hyperplasia [7]. Multiple studies investigate the mechanisms of ISR, such as Goto et al showing that the process of neointimal hyperplasia is the main cause of ISR in both BMS and DES, stent

underexpansion was greater in DES-ISR, and stent fracture was found only in DES-ISR [8].

Our study evaluates the prevalence of significant ISR of DES at 11% and shows a significantly higher value in those implanted in RCA as compared to those implanted in Cx and LAD. This is the first study that investigates the relationship between significant ISR and the corresponding culprit coronary artery.

Alfonso et al investigated different generations of stents revealing an overall rate of significant ISR around 12% [9]. In addition, Dangas et al reveals a rate of significant ISR in DES between 3-20% [10]. Giacoppo et al indicates that current rates on ISR are higher than 10% [11]. Buccheri et al shows an incidence of restenosis between 7-41% with BMS and less than 10% with DES [12]. Cassese et al studied a large cohort population and estimated the rate of DES-ISR to be higher than 10% [13]. These results found in literature review were similar to the results showed in our study (11%). DES were the only generation investigated due to strict inclusion criteria and the exclusion of all patients treated with other generation of stents. Our study was interested with DES because it is the most common used stent worldwide in our days whereas BMS and other type of stents are rarely used.

Zhao et al investigated the correlation between the rate of ISR and the number of involved coronary arteries and showed a higher rate of ISR in patients with two or more vessel disease as compared to patients with single vessel disease [14]. Our study investigates the correlation between the rate of ISR and the underlying involved coronary artery and shows a higher incidence of DES restenosis in patients with RCA disease as compared to patients with LAD or Cx disease. In addition, this study shows a statistically significant negative correlation between the rate of ISR and LAD stents insertion, and a positive correlation between the rate of ISR and RCA stents insertion.

5. Conclusion

This study evaluates the prevalence of DES-ISR at 11% with highest rate for stents placed in RCA as compared to stents implanted on other coronaries and it shows a significant positive relationship between the prevalence of ISR and RCA as an involved culprit coronary artery. We recommend a strict clinical follow-up of patients with RCA lesion treated by DES insertion and earlier invasive follow-up to prevent the complications due to ISR that can increase morbidity and mortality, especially in symptomatic patients.

List of Abbreviations

ISR: In stent restenosis.
 CAD: coronary artery disease.
 PCI: percutaneous intervention.
 DES: drug eluting stent.
 LAD: left anterior descending.

Cx: circumflex.

RCA: right coronary artery.

BMS: bare metallic stent.

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