Outcomes of On-Label Versus Off-Label Use of Drug-Eluting Coronary Stents: The Philippine Heart Center Clinical Practice

Kathleen G. Go, MD; Alexander Ang, MD; Ramoncito Tria, MD; James Ho, MD; Vergel Quiogue, MD

Background --- The use of drug-eluting stents have been approved based on data from several randomized controlled trials on simple de-novo lesions involving low-risk clinically stable patients with low lesion complexity with the more complex lesions or above-average risk clinical situations were excluded in these trials. But recent clinical practice quickly moved beyond the evidence on which approval had been based and included high-risk groups of patients that had not been studied in adequately sized clinical trials. This study was conducted to determine the frequency, safety, effectiveness and outcome of patients undergoing percutaneous coronary interventions (PCI) following off-label versus on-label use of drug eluting stents.

Methods --- This study employed an observational, prospective cohort study design and involved consecutive patients who underwent percutaneous coronary intervention with stenting between April 1, 2007 and November 30, 2007 at the Philippine Heart Center Invasive Cardiology Laboratory. Drug-eluting stents available and used included the Cypher Sirolimus-Eluting Stents, Taxus Paclitaxel-Eluting Stents, Endeavor Rapamycin-Eluting Stents, Firebird Rapamycin-Eluting Stents, Axxion Glycocalix and Paclitaxel-Eluting Stents and Xience V Everolimus Eluting Stents. Patients were grouped into On-Label Use for those whose indications are within the instructions for use stated for each of the respective stents. Procedures done beyond the stated indications were under Off-Label Use. Patients were followed up for a period of three months to observed for procedural and clinical outcomes at in-hospital, thirty-days and three months after the index procedure

Results ---Of the 352 patients who received drug-eluting stent, 248 (70.5%) had at least 1 off-label indication. Prior history of myocardial infarction and the number of diseased vessels are associated with the use of drug-eluting stents with a P-value of 0.033 and 0.000, respectively. Majority of the patients had chronic stable angina as the primary indication for the index procedure, 63.7% for off label use and 71.1% for on label use. Off-label use of drug eluting stents is strongly associated with having lesion length greater that 30 mm, reference vessel diameter greater than 3.5 mm or less that 2.5 mm, ostial lesions, bifurcation stenting and total occlusion. The mean lesion length of off-label is 34.3 mm while that of on-label is 19.6 mm. These are significantly different with p-value of 0.000. The average maximum lengths of stent used by both groups differ significantly. The mean number of lesions per patient for off-label (2.1) and on-label (1.3) are significantly different (p-value 0.000). The incidence rates of death, myocardial infarction, stent thrombosis, repeat PCI or CABG for target lesion revascularization were higher in the off label group compared to no events under the on-label group. Among the patients in the off-label group, 7 died while still in the hospital while 3 more died within 30 days from the procedure giving a mortality rate of 4%. None among the on-label group expired. Off- and on-label use of drug eluting stents is not associated with any of the procedural and clinical outcome

Conclusion --- Off-Label use of drug-eluting stents is more common than on-label use. Prior myocardial infarction, presence of graft stenosis and ST elevation MI shows significant association with off-label use of drug eluting stents. Off-label use of drug-eluting stents is associated with higher rates of adverse procedural and clinical outcomes during in-hospital stay, at 1 month and at 3 months. ***Phil Heart Center J 2008; 14(1):1-7.***

Key Words: Percutaneous Coronary Intervention (PCI) ■ Drug-eluting stents (DES) ■ Off-label use

Drug-eluting stents (DES) are considered a break through technology in the field of Cardiology. Since it was introduced, it has been used in a vast majority of Percutaneous Coronary Interventions (PCIs) around the world, including the Philippines. The approval from the US Food and Drug Administration

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Correspondence to Kathleen G. Go, MD. Division of Adult Cardiology. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100
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(US FDA) for the commercialization of the DES was based on data from several randomized controlled trials on simple de-novo lesions that either assesses angiographic or clinical outcomes such as target vessel revascularization.[1] Its approval was based on low-risk clinically stable patients with low lesion complexity with the more complex lesions or above-average risk clinical situations were excluded in these trials. Originally in April 2003, the Cypher Sirolimus-eluting coronary stents were approved for discrete de novo lesions of length < 30 mm in native coronary arteries with a reference vessel diameter (RVD) of > 2.5 to < 3.5 mm. In March 2004, the Taxus Express Paclitaxel-Eluting Coronary Stent System was approved for the treatment of de novo lesions < 28 mm in length in native coronary arteries > 2.5 to < 3.75 mm in diameter.[2] However, the uptake of drug-eluting stents into clinical practice quickly moved beyond the evidence on which approval had been based and included high-risk groups of patients that had not been studied in adequately sized clinical trials.[3-6] Therefore, the use of DES outside the FDA approved indications are considered off-label and these include: 1) de novo lesions with RVD 2.25 mm of 4 mm; maximum lengths 46 mm, chronic total occlusion with Class 1B evidence; 2) bifurcations (provisional stenting), ostial lesions, multi-vessel disease, and saphenous vein graft with Class IIaB evidence; 3) Bifurcation (two stent technique SB > 2.5 mm + ostial involvement), DES for in-stent restenosis of DES with Class IIaC evidence; and 4) Bifurcation (two stent technique Crushed, Cullotte, T-Stent; ultralong lesions (Full Metal Jacket), unprotected left main coronary artery disease, multi-vessel disease (complex and diffuse) and acute myocardial infarction with Class IIbB evidence.[7] To date, there is limited data as to outcome of using DES for off-label indications. This study evaluated the frequency, effectiveness, and safety of off-label use of DES in a prospective registry which would reflect "real-world" clinical practice here in the Philippine Heart Center.

Review of Related Literature

The U.S. FDA stated that off–label use of DES is associated with an increased risk of stent thrombosis, death or MI compared to off-label use. Data on off-label use are limited, and additional studies are needed to determine optimal treatments for more complex patients. Until more data are available, the DES labels should state that when DES are used off-label, patient outcome may not be the same as the results observed in the clinical trial conducted to support marketing approval.[2] But it has been observed that majority of the DES used in this institutions are for off-label indications. This is also true in foreign centers. Off-label situations make-up the bulk of usage, ranging from 60-75%.8 In the D.E.S. cover Registry, Boehar and colleagues reported 1-year results for 55541 patients in the registry, involving subjects from 140 US academic and community hospitals. In all, 47% of patients observed received stents for either an off-label or untested indication. Target lesion revascularization rates were significantly higher at 1 year in both off-label and untested use patients‟ however, the 1 year risk for death, myocardial infraction, or stent thrombosis was not statistically greater in off-label-use or untested-use patients as compared with on-label use patients, despite early, 30-day differences for both groups as compared with on-label patients.[6,9-10] In the EVENT Registry on the other hand, out of the 3323 patients who underwent stenting with DESs, 54.7% had at least 1 "off label" characteristics. During the index hospitalization, the composite clinical outcome of death, MI or target lesion Revascularization occurred in 10.9% in the off-label group and 5% in the on-label group (adjusted odds ratio, 2.32; 95% CI, 1.75-3.07; P<0.001). At 1 year, the composite clinical outcome occurs more often in the off-label group compared with the on-label group; 17.5% vs. 8.9%, (adjusted hazard ratio, 2.16; 95% CI, 1.74-2.67; P<0.001). Stent thrombosis also occurred more frequently among patients in the off-label group during the initial hospitalization (0.4% vs. 0) and at 1 year: 1.6% vs. 0.9%, adjusted HR, 2.29 (95% CI, 1.02-5.16; P=0.05).[3] Rao and colleagues showed in their study involving 408,033 procedures using DES, 24.1% had off-label indications. It was associated with low rate of short term adverse events.[4]

Significance

This study aims to evaluate the frequency, effectiveness, and safety of DES used for off-label indications in patients admitted at the Philippine Heart Center. Prospective documentation of this clinical experience will extensively document the demographic and clinical characteristics of the patients as well as the frequency of DES use in off-label clinical and angiographic situations, in-hospital, thirty-day and three-month outcome. A comprehensive registry such as this will provide a local hospital-based data that will serve as basis for future surveillance and researches geared towards patients requiring DES.

Research Question

What are the outcomes of patients undergoing percutaneous coronary intervention following off-label versus on-label use of drug eluting stents in the Philippine Heart Center?

Objectives

General Objective

To determine the outcomes of patients undergoing percutaneous coronary intervention following off-label versus on-label use of drug eluting stents in the Philippine Heart Center Specific Objectives

1. To determine the frequency of on-label and off-label use of drug eluting stents in percutaneous coronary intervention.
2. To determine the clinical profile of patients undergoing on- versus off-label drug-eluting stent in percutaneous coronary interventions
3. To determine index procedural characteristics
4. To compare the procedural and clinical outcomes between the on-label group and off-label group during the initial hospitalization.
5. To compare the procedural and clinical outcomes between the on-label group and off-label group 30 days after the procedure.
6. To compare the procedural and clinical outcomes between the on-label group and off-label group 3 months after the procedure.

Methods

This study employed an observational, prospective cohort design and included consecutive patients who underwent percutaneous coronary intervention from April 1, 2007 to November 30, 2007 at the Philippine Heart Center, a tertiary specialized center at Quezon City, Philippines. Patients who underwent percutaneous coronary intervention using bare metal stents only, balloon angioplasty only, aborted procedures and those with incomplete revascularization were not included in the study.

All consecutive patients who underwent percutaneous coronary intervention using drug eluting stents were enrolled and necessary demographic and clinical data were recorded. DES included in the study were those available in our institution which were as follows: 1) Cypher Sirolimus-Eluting Stents, 2) Taxus Paclitaxel-Eluting Stents, 3) Endeavor Rapamycin-Eluting Stents, 4) Firebird Rapamycin-Eluting Stents, 5) Axxion Glycocalix and Paclitaxel-Eluting Stents and 6) Xience V Everolimus Eluting Stents.

Patients were grouped according to the use of DES whether on-label or off-label. Off-label is defined on the basis of the directions for use of the Cypher, Taxus, Endeavor, Firebird, Axxion and Xience V drug-eluting stents available in the Cardiovascular Laboratory of the Philippine Heart Center. The Cypher stent directions for use state that it is indicated for "improving the coronary luminal diameter in patients with symptomatic ischemic disease due to discrete de novo lesions of length < 30 mm in native coronary arteries with reference vessel diameter of > 2.5 and <3.5 mm." The Taxus stent directions for use state that it is indicated for "improving luminal diameter for the treatment of de novo lesions < 28 mm in length in native coronary arteries > 2.5 to < 3.75 mm in diameter." The Endeavor stent directions for use state that it is indicated "for improving coronary luminal diameter and reducing restenosis in patients with symptomatic ischemic heart disease in de novo coronary artery lesions in native coronary arteries with a reference vessel diameter of 2.25 mm to 4.0 mm and a lesion length of < 27 mm". The Firebird stent directions for use state that it is indicated "for improving coronary luminal diameter in patients with symptomatic ischemic disease due to discrete de novo lesions of lengths <30mm in native coronary arteries with a reference vessel diameter of > 2.5 to < 4.0 mm." The Xience V stent direction for use state that it is indicated "for improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to discrete de novo native coronary artery lesions of lengths < 28 mm and a reference vessel diameter of 2.5 -4.0 mm." The uses of these stents outside the "recommended indications for use" are considered off-label.

Aside from the lengths and diameter sizes previously mentioned, other off-label use are as follows: chronic total occlusion, bifurcations (provisional stenting), ostial lesions, multi-vessel disease, and saphenous vein graft, bifurcation (two stent technique SB > 2.5 mm + ostial involvement), DES for in-stent restenosis of DES and bifurcation (two stent technique Crushed, Cullotte, T-Stent; ultralong lesions (Full Metal Jacket), unprotected left main coronary artery disease, multi-vessel disease (complex and diffuse) as well as acute myocardial infarction.

Clinical profile, including age, gender, smoking history, hypertension, diabetes mellitus, chronic renal insufficiency, chronic lung disease, congestive heart failure, myocardial infarction, peripheral vascular disease, previous PCI, previous CABG, number of diseased vessels, number of graft stenoses and primary indication for the index procedure were assessed. Angiographic features in terms of off-label indications, number of lesions per patient, lesion length in mm, reference vessel diameter in mm, de novo lesion, lesion location, TIMI flow, direct stenting, stent overlap, maximum length of stent use as well as angiographic success were also assessed. Procedural and clinical events in terms of death, myocardial infarction, stent thrombosis, repeat PCI for target lesion revascularization and CABG surgery hospitalization, at 30 days and 3 months after discharge were also assessed.

Sample Size

At a confidence interval of 95% and power to detect a significant difference of 80% with an assumed outcome rate of 14.7% in the off-label group and 6.8% in the on-label group, N should be greater than or equal to 530 patients.

Statistical Analysis

Patients under the Off-Label group were compared with that of the On-Label group. The data was analyzed with results presented as frequency and percent distribution. T test was used for continuous variables and X2 test will be used for categorical variables. A P value of < 0.05 was considered statistically significant. The odds ratio (OR) and its 95% confidence interval for each factor were presented.

Results

Patient Population Two hundred forty eight (70.5%) of the 352 patients who received drug-eluting stents included in this study had at least one off-label indication. Table 1 gives the comparison of the clinical profile of patients who had on- and off-label indications for the use of DES. Prior history of myocardial infarction is strongly associated with off-label use while single vessel disease is strongly associated with on-label use with a p-value of 0.033 and 0.000, respectively. The rest of the baseline characteristics are comparable in both groups.

Table 1. Clinical Profile of Patients included in the Study

Clinical Profile	Off-label N= 248	On-label N=104
Age, y	60.9 ± 11.4	60.6 ± 11.2
Sex		
Male, n (%)	191 (77.0)	75 (72.1)
Female, n (%)	57 (23.0)	29 (27.9)
HPN, n (%)	187 (75.4)	75 (72.1)
DM, n (%)	89 (35.9)	42 (40.4)
Smoking, n (%)	69 (27.8)	24 (23.1)
MI, n (%)	67 (27.0)	18 (17.3)**
CHF, n (%)	20 (8.1)	9 (8.7)
CRI, n (%)	5 (2.0)	0 (0.0)
COPD, n (%)	4 (1.6)	1 (1.0)
Prior PCI, n (%)	18 (7.3)	5 (4.8)
Prior CABG, n (%)	13 (5.2)	1 (1.0)
Graft Stenosis, n (%)	3 (1.2)	0 (0.0) **
Number of Diseased Vessels		
1, n (%)	135 (54.4)	84 (78.8) **
2, n (%)	87 (35.1)	16 (15.4)
3, n (%)	26 (10.5)	6 (5.8)

*Data are presented as mean ± SD or No. (%) unless otherwise indicated.
** association

ST-Elevated myocardial infarction and off-label use of drug eluting stents are associated with p-value 0.048. (Table 2)

Table 2. Primary Indication of Index Procedure

Primary Indication of Index Procedure	Off-label N=248	On-label N=104
STEMI, n (%)	50 (20.2)	13 (12.5)**
UA/ NSTEMI, n (%)	27 (10.9)	11 (10.6)
CSA, n (%)	158 (63.7)	74 (71.1)
Ischemia on work-up, n (%)	13 (5.2)	6 (5.8)

*Data are presented as no. (%) unless otherwise indicated.
** association

Procedural and Lesion Characteristics Table 3 presents the off-label indications. Off-label use of drug eluting stents is strongly associated with having lesion length greater that 30 mm, reference vessel diameter greater than 3.5 mm or less that 2.5 mm, ostial lesions, bifurcation stenting and total occlusion with p-value of 0.000 except for ostial which has p-value of 0.014. The mean number of lesions per patient for off-label (2.1) and on-label (1.3) are significantly different (p-value 0.000). (Table 4)

Table 3. Frequency of the Off-label Indications included in this study

Off-label Indications	Off-label n-248	On-label n-104
Lesion length > 30	162 (65.3)	0 (0.0)**
RVD > 3.5	46 (18.5)	0 (0.0)**
RVD < 2.5	92 (37.1)	0 (0.0)**
LM	4 (1.6)	0 (0.0)
Ostial	12 (4.8)	0 (0.0)**
Bifurcation	30 (12.1)	0 (0.0)**
Total Occlusion	25 (10.1)	1 (1.0)**
Restenosis	4 (1.6)	0 (0.0)
SVG	2 (0.8)	0 (0.0)

*Data are presented as n (%).
** association

The mean lesion length of off-label is 34.3 mm while that of on-label is 19.6 mm. These are significantly different with p-value of 0.000. Similarly, the average maximum lengths of stent used by both groups differ significantly. Off-label use of drug eluting stents is strongly associated with right coronary artery lesion, left circumflex artery lesion, pre-procedural TIMI flow, direct stenting and stent overlap. On-label use of drug eluting stents is strongly associated with de novo lesions. (Table 5)

Table 4. Overall Index Procedural Characteristics of PCI patients who underwent either On-label or Off-label Stenting

Overall Index Procedural Characteristics	Off-label n-248	On-label n-104
Number of Lesions per patient	2.1 ± 0.9	1.3 ± 0.6 **
Multivessel PCI, n (%)	92 (37.1)	17 (17.3)
Stents Used, Total n, %	549 (80.5)	133 (19.5)
Taxus, %	44.7	57.9
Firebird, %	32.5	20.3
Cypher, %	4.4	9.0
Axxion, %	6.1	5.2
Genous, %	7.0	2.1
Endeavor, %	3.5	4.5
Xience V, %	1.8	1.0

*Data are presented as mean ± SD or No. (%) unless otherwise indicated.

** significantly different

Table 5. Lesion Level Index Procedural Characteristics of PCI patients who underwent either On-label or Off-label Stenting

Lesion Level Index Procedural Characteristics	Off-label n-248	On-label n-104
Lesion length, mm	34.3 ± 15.2	19.6 ± 5.3†
RVD, mm	2.9 ± 1.9	2.7 ± 0.2
De Novo Lesions, n (%)	28 (11.3)	67 (64.4)**
RCA, n (%)	110 (44.4)	30 (28.8)**
LAD, n (%)	181 (73.0)	76 (73.1)
LCX, n (%)	82 (33.1)	17 (16.3)**
LM, n (%)	4 (1.6)	1 (1.0)
SVG, n (%)	2 (0.8)	0 (0.0)
Pre-procedural TIMI flow		
0, n (%)	31 (12.5)	0 (0.0)**
1, n (%)	2 (0.8)	0 (0.0)
2, n (%)	22 (8.9)	16 (15.4)
3, n (%)	193 (77.8)	87 (83.7)
Post-procedural TIMI flow		
2, n (%)	1 (0.4)	0 (0.0)
3, n (%)	247 (99.6)	104 (100)
Direct Stenting	203 (81.9)	72 (69.2)**
Stent Overlap, n (%)	93 (37.5)	2 (1.9)**
Maximum length of stent used	34.7 ± 15.6	20.1 ± 4.9†
Angiographic Success, n (%)	247 (99.6)	104 (100%)

*Data are presented as mean ± SD or No. (%) unless otherwise indicated.

†significantly different

**associated

Observed In-Hospital, 30-Day and 3-Month Outcomes
The incidence rates of death, myocardial infarction, stent thrombosis, repeat PCI or CABG for target lesion revascularization were higher in the off label group compared to no events under the on-label group. Among the patients in the off-label group, 7 died while still in the hospital while 3 more died within 30 days from the procedure giving us an in-hospital mortality rate of 2.8%, 30-day mortality rate of 1.2% and overall mortality rate of 4%. None among the on-label group expired. Off- and on-label use of drug eluting stents is not associated with any of the procedural and clinical outcome. (Table 6)

Table 6. Procedural and Clinical Outcome (In-Hospital, 30 days and 3-months) of PCI patients who underwent either Off-label or On-label stenting

Procedural and Clinical Outcome	Off-label n-248	On-label n-104
In Hospital		
Death, n (%)	7 (2.8)	0 (0.0)
MI, n (%)	3 (1.2)	0 (0.0)
Stent Thrombosis, n (%)	6 (2.4)	0 (0.0)
Repeat PCI, n (%)	3 (1.2)	0 (0.0)
CABG, n (%)	0 (0.0)	0 (0.0)
Target Vessel Revascularization via PCI or CABG	3 (1.2)	0 (0.0)
Death or MI	10 (4.0)	0 (0.0)
Death, MI, or Stent Thrombosis	16 (6.4)	0 (0.0)
30 days		
Death, n (%)	3 (1.2)	0 (0.0)
MI, n (%)	0 (0.0)	0 (0.0)
Stent Thrombosis, n (%)	0 (0.0)	0 (0.0)
Repeat PCI, n (%)	1 (0.4)	0 (0.0)
CABG, n (%)	0 (0.0)	0 (0.0)
Target Vessel Revascularization via PCI or CABG	3 (1.2)	0 (0.0)
Death or MI	3 (1.2)	0 (0.0)
Death, MI, or Stent Thrombosis	3 (1.2)	0 (0.0)
3 Months		
Death, n (%)	0 (0.0)	0 (0.0)
MI, n (%)	1 (0.4)	0 (0.0)
Stent Thrombosis, n (%)	0 (0.0)	0 (0.0)
Repeat PCI, n (%)	1 (0.4)	0 (0.0)
CABG, n (%)	1 (0.4)	0 (0.0)
Target Vessel Revascularization via PCI or CABG	2 (0.8)	0 (0.0)
Death or MI	1 (0.4)	0 (0.0)
Death, MI, or Stent Thrombosis	1 (0.4)	0 (0.0)

Discussion

Data in this study showed that the frequency of off label use of drug eluting stents (70.5%) was much higher compared to the 47% in the D.E.S. cover Registry [6,9] and the 54.7% in the EVENT Registry [5,9]. In both international registries, only those given Paclitaxel-eluting stents and Sirolimus-eluting stents were included. Our study, on the other hand, included 7 different drug eluting stents which are regularly used in our laboratory, giving us a more "real world" picture of this institution's clinical practice.

The EVENT Registry[5] showed that the male gender, congestive heart failure, prior history of myocardial infarction and coronary artery bypass graft, acute coronary syndromes as procedural indication were significantly associated with off-label use of DES. Positive stress test was significantly associated with on-label use of DES. In our study, however, prior history of myocardial infarction and STEMI as procedural indication are strongly associated with off-label use of DES while single vessel disease is strongly associated with on-label use of DES with a p-value of 0.033, 0.048 and 0.000, respectively. The rest of the baseline characteristics are comparable for both groups.

Despite high rates of angiographic success in the off-label group in this study, the incidence rates of death, myocardial infarction, stent thrombosis, repeat PCI or CABG for target lesion revascularization as well as composite outcome were higher in the off label group compared to no events under the on-label group. This was compatible with the results of the EVENT Registry showing that off-label status was the strongest predictor of both in-hospital and 1 year adverse cardiac events. It was also associated with higher risk of stent thrombosis, 0.4% in the EVENT Registry and 2.4% in our study. Among the patients in the off-label group, 7 died while still in the hospital while 3 more died within 30 days from the procedure giving us an in-hospital mortality rate of 2.8%, 30-day mortality rate of 1.2% and overall mortality rate of 4% in this study. None among the on-label group expired. The difference may probably be due to higher acute myocardial infarction cases in the off-label group. The D.E.S. cover Registry reported that adjusted in-hospital risk of death, MI, or stent thrombosis was not statistically different with off-label or untested vs. standard use. At 30 days, the risk of this composite endpoints was significantly higher with off-label use (adjusted hazard ratio [HR], 2.08; 95% CI, 1.24-3.48; P=0.005). Excluding early events, this end point was not different at 1 year with off-label use (adjusted HR, 1.10; 95% CI, 0.79-1.54; P=0.57). At one year, compared to with standard use, significantly higher rates of target vessel revascularization were associated with off-label use (adjusted HR, 1.49; 95% CI, 1.13-1.98; P=0.005). The EVENT Registry on the other hand showed that the composite outcome occurred during the index hospitalization in 10.9% of patient in the off-label group and in 5% of patients in the on-label group (adjusted odds ratio, 2.32, 95% CI, 1.75-3.07; P <0.001). At one year, the composite clinical outcome occurred more often in the off-label group than in the on-label group: 17.5% vs. 8.9%, adjusted HR, 2.16; 95% CI, 1.74-2.67; P <0.001). Stent thrombosis was also more frequent in the off label group during initial hospitalization (0.4% vs. 0) and at one year (1.6% vs. 0.9%); adjusted HR, 2.29; 95% CI, 1.02-5.16, P=0.05).

Results in this study should be interpreted with several caveats. Although all patients who qualified were included, the number is significantly low compared to international registries. Comparison with of patients receiving DES off-label concurrent with that of patients receiving bare-metal stents and those undergoing bypass for the same procedural indications was not done in this study. Compliance to patient's treatment regimen, most specifically the antiplatelets aspirin and clopidogrel, was not investigated in this study. Follow-up was only limited to three months from the index procedure, therefore, long-term outcomes will not be answered by the results of this study.

Conclusion

Off-Label use of drug-eluting stents is more common than on-label use. Prior myocardial infarction, presence of graft stenosis and ST elevation MI shows significant association to off-label use of drug eluting stents. Off-label use of drug-eluting stents is associated with higher rate of adverse procedural and clinical outcomes during in-hospital stay, at 1 month and at 3 months.

References

1. Roiron C, Sanchez P, Bouzamondo A, Lechat P, Montalescot G. Drug eluting stents an updated meta-analysis of randomized controlled trials. *Heart 2006;92:641-649.*
2. Administration Fad: *http//www.fda.fov/cdm/news/010407 html.2006.*
3. Harrington R, Ohman E. The enigma of drug-eluting stents: Hope, Hype, Humulity, and Advancing Patient Care. *JAMA 2007;297(8):2028-2030.*
4. Rao SV, Shaw RE, Brindis RG, et al. On- versus off-label use of drug-eluting coronary stents in clinical practice (report from the American College of Cardiology National Cardiovascular Data Registry [NDCR]. *Am J Cardiol 2006;97:1478-1481.*
5. Win H, Caldera A, et al. Clinical outcomes and stent thrombosis following off-label use of drug eluting stents. *JAMA 2007;297(8):2001-2009.*
6. Beohar N, Davidson C et al. Outcomes and complications associated with off-label and untested use of drug eluting

stents. *JAMA 2007;297:(18):1992-2000.*
7. Ramcharita S, Serruys P. Drug-eluting stents: indications, limits and future developments. *Cardiology International 2007;8(2):49-55.*
8. Wood S. Day 2: FDA panel warns against increased risk of death/MI, stent thrombosis with off-label DES use. *http//www.theheart.org. December 11, 2006.*
9. Wood S. Off-label drug-eluting stent use linked with increased repeat Revascularization CME. *http://www.medscape.com/viewarticle/556358 May 11, 2007*
10. Williams DO, Abbott JD, Kip DE; DEScover Investigators. Outcome of 6906 patients undergoing percutaneous coronary intervention in the era of drug-eluting stents: reports of the DEscover Registry. *Circulation 2006; 114:2154-2162.*

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