

## Efficacy Of Drug Eluting Stents Versus Cobalt Chromium Stents In Small Coronary Artery Stenosis In Non Diabetic Patients

Yasser Elsayed Mohammed, Ahmed Roza, Saad Elzogby, Abdelrahman Aly and Mostafa Mokarab

Cardiology Department, Faculty of Medicine, Al-Azhar University

[Yasserelsayed@yahoo.com](mailto:Yasserelsayed@yahoo.com)

**Abstract:** At present, coronary artery disease (CAD) is one of the leading causes of death and disability in the developed world. According to the American Heart Association CAD was responsible for approximately 445,687 deaths in the United States in 2005, representing 20% of all deaths that year. Over the past two decades, percutaneous transluminal coronary angioplasty (PTCA) with bare-metal stent (BMS) placement has been utilised as a minimally invasive treatment for obstructive CAD. Treatment with a BMS will generally result in extremely favourable initial clinical results. However, at follow-up (6–12 months), re-narrowing of the treated artery is commonly observed in 20–30% of patients. This re-narrowing of the treated artery is due to in-stent restenosis (ISR). In recent years, DESs have been developed to address the problem of ISR. A DES typically consists of a BMS platform which has been coated in a formulation of drugs and carrier materials. Percutaneous coronary interventions (PCI) in small coronary arteries represent up to 35% of all catheter-based procedures in the daily practice. In particular, the rates of stent restenosis in the small vessel scenario are markedly higher when compared with stent restenosis rates in large vessels. We studied 100 patients with stable coronary artery disease subjected for elective PCI as all patients had single vessel disease and according to type of stent used in intervention, the patients were classified into 50 patients with drug eluting stents to treat de novo coronary lesions and 50 patients with cobalt chromium stents to treat de novo coronary lesions. The results of this study showed that, the use of drug eluting stent versus cobalt chromium stent was associated with a significant reduction in target vessel revascularization in small artery stenosis through 1-year follow-up with no difference in death, nonfatal myocardial infarction. The conclusion from our results suggested that the no difference in death, nonfatal myocardial infarction between drug eluting stent versus cobalt chromium stent and TVR was reduced.

[Yasser Elsayed Mohammed, Ahmed Roza, Saad Elzogby, Abdel rahman Aly and Mostafa Mokarab. **Efficacy Of Drug Eluting Stents Versus Cobalt Chromium Stents In Small Coronary Artery Stenosis In Non Diabetic Patients.** *J Am Sci* 2015;11(1):78-87]. (ISSN: 1545-1003). <http://www.jofamericanscience.org>. 11

**Keywords:** Drug; Stents; Cobalt Chromium; Coronary Artery Stenosis; Diabetic Patient

### 1. Introduction

At present, coronary artery disease (CAD) is one of the leading causes of death and disability in the developed world. According to the American Heart Association CAD was responsible for approximately 445,687 deaths in the United States in 2005, representing 20% of all deaths that year (Lloyd-Jones *et al.*, 2009).

Over the past two decades, percutaneous transluminal coronary angioplasty (PTCA) with bare-metal stent (BMS) placement has been utilised as a minimally invasive treatment for obstructive CAD. Typically, a BMS is a small, tubular, wire-mesh device which is pre-loaded in a collapsed form onto a catheter balloon, threaded to the narrowed section of the artery and expanded within the vessel. Once expanded, the BMS acts as a mechanical scaffold, reducing elastic recoil and maintaining vessel patency post-treatment. For many patients who suffer from CAD, treatment with a BMS will generally result in extremely favourable initial clinical results. However, at follow-up (6–12 months), re-narrowing of the treated artery is commonly observed in 20–30% of patients (Fischman

*et al.*, 1994). This re-narrowing of the treated artery is due to in-stent restenosis (ISR) which is defined as diameter stenosis of  $\geq 50\%$  in the stented area of the vessel (Cutlip *et al.*, 2002).

In recent years, DESs have been developed to address the problem of ISR. A DES typically consists of a BMS platform which has been coated in a formulation of drugs and carrier materials. The drugs commonly employed are known to interrupt the key cellular and molecular processes associated with ISR. To date, clinical evaluation has overwhelmingly proven the superiority of DESs for the reduction of ISR rates compared to BMSs, leading to the regulatory approval of a number of DESs by both the European Union (EU) Conformité Européenne (CE) and the US Food and Drug Administration (FDA). Despite the success of DESs in the treatment of CAD, concern has arisen over the long-term safety and efficacy of these devices due to cases of late adverse clinical events such as stent thrombosis. With this concern in mind, research and development in DES design is currently centered on increasing their performance and long-term safety.

The introduction of the drug-eluting stent (DES) proved to be an important step forward in reducing rates of restenosis and target lesion revascularization after percutaneous coronary intervention. However, the rapid implementation of DES in standard practice and expansion of the indications for percutaneous coronary intervention to high-risk patients and complex lesions also introduced a new problem: DES in-stent restenosis (ISR), which occurs in 3% to 20% of patients, depending on patient and lesion characteristics and DES type. The clinical presentation of DES ISR is usually recurrent angina, but some patients present with acute coronary syndrome. (George *et al.*, 2010).

Percutaneous coronary interventions (PCI) in small coronary arteries represent up to 35% of all catheter-based procedures in the daily practice (Morice *et al.*, 2003).

Despite their high frequency, there is a well defined inverse correlation between acute and long-term success and reference vessel diameter, meaning that patients with lesions in small coronary arteries are at higher risk of procedure failure and adverse events during their follow-up (Hsieh *et al.*, 2001).

In particular, the rates of stent restenosis in the small vessel scenario are markedly higher when compared with stent restenosis rates in large vessels (Kastrati *et al.*, 2006).

Currently, a majority of market-approved stents deployed in small coronary arteries have a higher metal-to-artery ratio, which might contribute to increasing local inflammatory response, thus also increasing the risk of subacute thrombosis and restenosis (Morice *et al.*, 2003).

## 2. Patients and Methods

We studied one hundred patients who had been admitted to AL-Azhar University Hospitals and Cairo Specialized Hospital with stable coronary artery disease for elective PCI between April 2011 and April 2013. All patients had single vessel disease. According to type of stent used in intervention, the patients were classified into group 1, included 50 patients with drug eluting stents to treat de novo coronary lesions, and group 2 included 50 patients with cobalt chromium stents to treat de novo coronary lesions.

Routine care before and after the procedure was done for all patients, including pretreatment with a loading dose of clopidogrel.

Patients were selected according to the following inclusion criteria, lesion length < 25 mm and Lesions diameter < 3mm, and exclusion criteria, diabetic patients, lesions longer than 25mm, Lesions with diameter more than 3mm, contraindication to aspirin or clopidogrel, post CABG, restenotic lesions and multivessels disease.

- **All patients were subjected to the following:** Informed consent, Complete History taking, Resting 12

leads ECG, C-reactive protein (CRP), clinical assessment: including cardiac examination and routine general examination.

- Echocardiography to assess the LV function and regional wall motion abnormalities (RWMAS).

- PCI by drug eluting stents and cobalt-chromium stents to small artery stenosis with diameter less than 3mm and length less than 25mm.

- Follow-up by coronary angiography to detect presence of in-stent restenosis within 6 months.

### Statistical analysis of data:

Data were analyzed using the SPSS program version 15. Continuous variables were expressed by mean  $\pm$  SD, while categorical variables were expressed in frequencies and percentages. Comparison between independent continuous variables was done by unpaired t-test. In case of unequal variances, Welch's modification was applied. Comparison between categorical variables was done by Chi square or Fisher's exact test as required. The Kaplan-Meier method was used to study the event free survival. Log-rank test was used to compare the survival of the 2 study groups. *P* value was considered significant if < 0.05.

## 3. Results

This study was conducted on one hundred patients who had been admitted to AL-Azhar University Hospitals and Cairo Specialized Hospital with stable coronary artery disease for elective PCI between April 2011 and April 2013. All patients had single vessel disease.

According to type of stent used in intervention, the patients were classified into 2 groups, group one included 50 patients with drug eluting stents to treat de novo coronary lesions and group two included 50 patients with cobalt chromium stents to treat de novo coronary lesions.

The study included 84 males and 16 females with mean age of  $57.09 \pm 9.84$  years (range: 35 – 85 years); 70 patients were hypertensive, 65 were smokers, 28 were obese, 72 were dyslipidemic, 30 had positive family history of coronary artery disease.

### Angiographic and procedural data:

Coronary artery disease included 42 patients with LAD lesions, 41 patients with LCX lesion and 17 patients with RCA lesions. Fourteen lesions were proximal, 56 lesions were mid and 30 were distal. Type A lesions were found in 73 patients, type B lesions in 26 patients, and type C lesion in 1 patient. The mean lesion severity was  $82.75 \pm 6.68$  %.

### Follow up data:

Major adverse cardiac events occurred in 7 patients; death in 2 patients, one of them during CABG and the other due to unknown cause, MI in 2 patients, one of them referred for CABG and TVR in 6 patients.

ISR occurred in 7 patients and 2 patients were referred for CABG.

The cumulative event free survival of the whole study population over the follow up period.

**Table 1: Baseline characteristics of the whole study population.**

	n=100
<b>Age(yrs)</b>	
Mean	57.09 ± 9.84
Range	35 – 85
<b>Gender</b>	
Male (no. %)	84 (84%)
Female (no.%)	16 (16%)
<b>HTN (n.%)</b>	70 (70%)
<b>Smoking (no.%)</b>	65 (65%)
<b>Obesity (no.%)</b>	28 (28%)
<b>Dyslipidemia (no.%)</b>	72 (72%)
<b>FH (no.%)</b>	30 (30%)
<b>Anginal Class*</b>	
Mean	2.93 ± 0.38
Range	2 – 4
<b>CRP (mg/L)</b>	
Mean	3.1 ± 8.71
Range	0.81 – 88
<b>EF (%)</b>	
Mean	56.83 ± 7.03
Range	45 – 68

### Comparison between the 2 study groups:

#### Baseline characteristics:

In group I, the mean age was 55.52 ± 7.48 years, while in group II was 58.66 ± 11.59 years, with no statistically significant difference between the 2 groups (p value=0.11). In group I five patients (5/50) were females while in group II eleven (11/50) were females with no significant difference between both groups (p value =0.17). Hypertension was more common in group II. In groups I and II hypertension was present in 86% and 54% respectively with significant difference between both groups (p value = 0.001).

**Table 2: Baseline angiographic and procedural data**

	n =100
<b>Coronary artery disease</b>	
LAD	42 (42%)
LCX	41 (41%)
RCA	17 (17%)
<b>Site of lesion</b>	
Proximal:	14 (14%)
LAD	7
LCX	5
RCA	2
MID:	56 (56%)
LAD	23
LCX	24
RCA	9
Distal:	30 (30%)
LAD	13

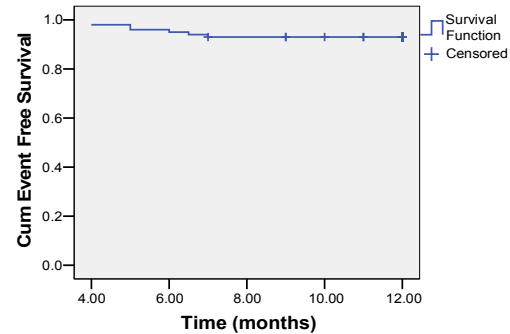
LCX	11
RCA	6
<b>Type of lesion</b>	
A	73 (73%)
B	26 (26%)
C	1 (1%)
<b>Lesion severity (%)</b>	
Mean	82.75 ± 6.68
Range	70 – 95
<b>Procedural data</b>	
Lesion length (mm)	
Mean	11.68± 3,73
Range	5 – 20
Reference diameter (mm)	
Mean	2.82 ± 0.08
Range	2.6 – 2.9
Stent diameter (mm)	
Mean	2.64 ± 0.12
Range	2.25 – 2.75
Stent length (mm)	
Mean	18.15± 4.12
Range	10 – 25
Inflation pressure (atm)	
Mean	14.42± 1.21
Range	12 – 16

LAD= left anterior descending artery, LCX= left circumflex artery, RCA= right coronary artery.

**Table 3: Follow up data**

	n= 100
<b>MACE (no., %)</b>	7 (7%)
<b>Death (no. %)</b>	2 (2%)
<b>MI (no. %)</b>	2 (2%)
<b>TVR (no. %)</b>	6 (6%)
<b>CABG (no. %)</b>	2 (2%)
<b>ISR (no. %)</b>	7 (7%)
<b>Severity of lesion on 2<sup>nd</sup> angiography(%)</b>	
Mean± SD	59.16± 27.64
Range	(20 – 95)

MACE=major adverse cardiac events, MI=myocardial infarction, TVR= target vessel revascularization, CABG=coronary aretery bypass graft, ISR= in-stent restenosis



Kaplan Meier curve showing the cumulative event free survival of the whole study sample.

Thirty three patients in group I(66%)and thirty two (64%) in group II were smokers, with no significant difference between the two groups ( $p$  value= 1.00).Fourteen patients in group I(28%)and fourteen patients (28%) in group II were obese with no significant difference between the two groups ( $p$  value = 0.82).

Forty patients (80%) had history of dyslipidemia in group I compared to thirty two (64%) in group II with no significance between the two groups ( $p$  value =0.11). Sixteen patients (32%) in group I and fourteen

(28%) in group II had a positive family history of coronary artery disease, with no statistical significance ( $p$  value =0.82). In group I, the mean angina class was  $2.94 \pm 0.31$  while in group II was  $2.92 \pm 0.44$ , with no significant difference between both groups ( $p$  value =0.79). In group, I the mean CRP was  $4.05 \pm 1.22$  while in group II was  $2.41 \pm 1.60$  with no statistically significant difference between both groups ( $p$  value = 0.27). In group I, the mean EF was  $57.32 \pm 6.7\%$  while in group II were  $56.34 \pm 7.39\%$ , with no significant difference between both groups ( $p$  value =0.48).

**Table 4: Baseline characteristic among the 2 study groups.**

	<b>Group 1 (DES)</b> n= 50	<b>Group 2 (CCS)</b> n= 50	<b>P value</b>
<b>Age (yrs)</b>	55.52 $\pm$ 7.48	58.66 $\pm$ 11.59	0.11
<b>Gender</b>			
Male (no, %)	45 (90%)	39 (78%)	0.17
Female (no, %)	5 (10%)	11 (22%)	
<b>HTN (no, %)</b>	43 (86%)	27 (54%)	0.001
<b>Smoking (no. %)</b>	33 (66%)	32 (64%)	1.0
<b>Obesity (no. %)</b>	14 (28%)	14 (28%)	0.82
<b>Dyslipidemia (no.%)</b>	40 (80%)	32 (64%)	0.11
<b>FH (no.%)</b>	16 (32%)	14 (28%)	0.82
<b>Angina class</b>	2.94 $\pm$ 0.31	2.92 $\pm$ 0.44	0.79
<b>CRP (mg/l)</b>	4.05 $\pm$ 1.22	2.41 $\pm$ 1.60	0.27
<b>EF%</b>	57.32 $\pm$ 6.7	56.34 $\pm$ 7.39	0.48

#### Angiographic and procedural data:

In group I, twenty lesions in LAD, twenty four in LCX, six in RCA, while in group II, twenty two lesions in LAD, seventeen in LCX, eleven in RCA, with no statistical significance ( $p$  value = 0.25). In group I, five lesions in the proximal part, thirty one in the mid part and fourteen in the distal part while in group II, nine lesions in the proximal, twenty five in the mid and sixteen in the distal part. There is no statistical significance ( $p$  value = 0.38). In group I, thirty six lesions (72%) were of type A, thirteen (26%) of type B and one (2%) of type C while in group II, thirty seven patients (74%) had type A, thirteen (26%) had type B and zero (0%) had type C with no statistical significance ( $p$  value =0.60).

In group I, the lesion severity ranged from 82.67 to 86.32 % with a mean  $84.5 \pm 6.4$  while in group II the lesion severity ranged from 79.13 to 82.86% with a mean  $81 \pm 6.54$ . There was significant difference between group I and group II according to lesion severity ( $p$  value =0.008). The mean lesion length of the studied group was  $12.44 \pm 3.81$  in group I and  $10.92 \pm 3.53$  in group II with statistical significance ( $p$  value = 0.04).

The mean reference diameter (RD) was  $2.83 \pm 0.7$  mm in group I and  $2.81 \pm 0.1$  in group II with no significant difference ( $p$  value = 0.21).

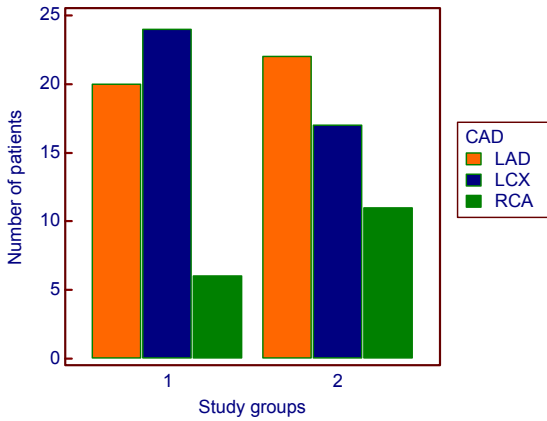
The mean stent diameter was  $2.65 \pm 0.12$  mm in group I and  $2.63 \pm 0.13$  mm in group II with no significant difference between the 2 groups ( $p$  value = 0.43). The mean stent length was  $18.54 \pm 3.99$  mm in group I and  $17.76 \pm 4.25$  mm in group II with no significant difference ( $p$  value = 0.34). The mean stent inflation pressure of the studied groups was  $14.6 \pm 1.16$  in group I and  $14.24 \pm 1.25$  in group II with no statistically significant difference ( $p$  value = 0.13).

#### Follow up data:

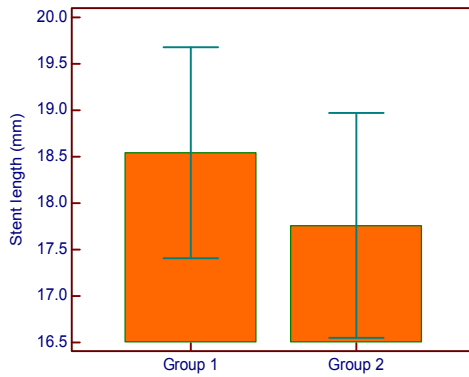
Major adverse cardiac events occurred in group I in three patients (6%) while in group II four patients (8%) with no statistical significance ( $P=1$ , odds ratio= 0.75, 95% CI = 0.17 – 3.81). One patient died during follow up period (during GABG) in group I and one patient in group II due to unknown cause with no significant difference ( $p$  value = 0.47). Two patients developed MI in group I but MI didn't occur in group II which is considered not significant ( $p$  value = 0.47). TVR occurred in group I in three patients (6%) and in the same number of patients in group II with no statistical significance ( $p$  value = 1.00, odds ratio = 1, 95% CI = 0.21 – 4.71).

CABG occurred in two patients (4%) in group I, while it didn't occur in group II with no statistical significance ( $p$  value = 0.07). In-stent restenosis occurred in group I in three patients (6%) while in

group II in four patients (8%) with no statistical significance ( $p$  value = 0.97, odds ratio= 0.73, 95% confidence interval = 0.17 – 3.11). There was significance difference between both groups as regard severity of lesion on 2<sup>nd</sup> angiography which is being higher in group I than group II ( $p$  value = 0.008).



Site of lesion among the 2 study groups ( $p=0.25$ ).



Comparison between stent length among the 2 study groups ( $p=0.34$ ).

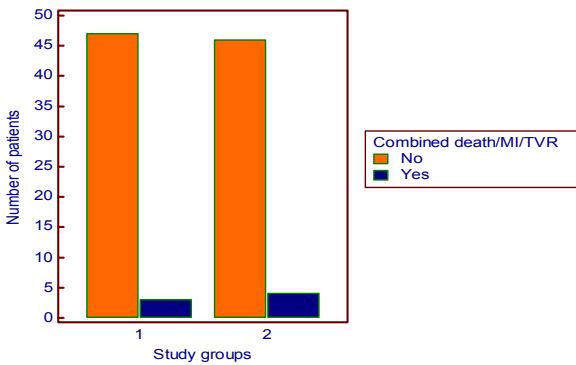
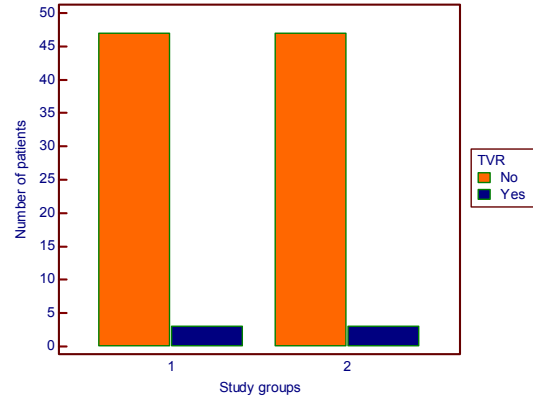
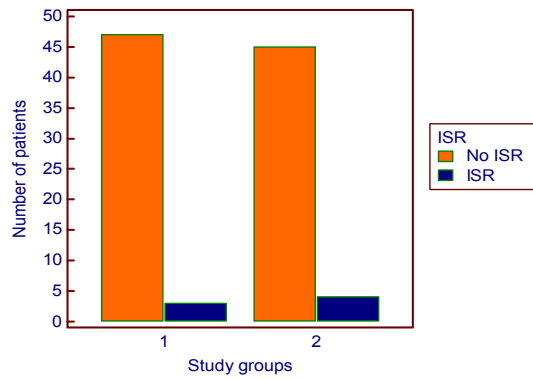


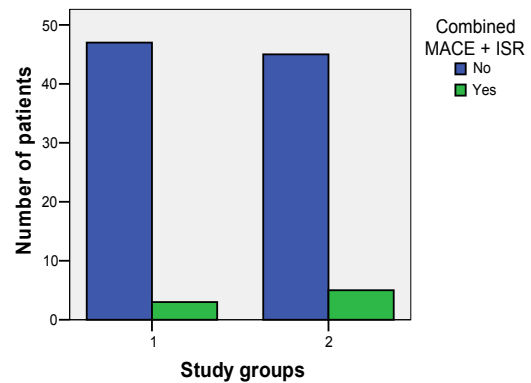
Figure (20): MACE among the study groups ( $p=1.00$ )



TVR among the study groups ( $p=1.00$ )



ISR among the study groups ( $p=0.97$ ).



Combined MACE + ISR among the study groups ( $p=0.71$ ).

**Table 5:** Angiographic and procedural data among the 2 study groups.

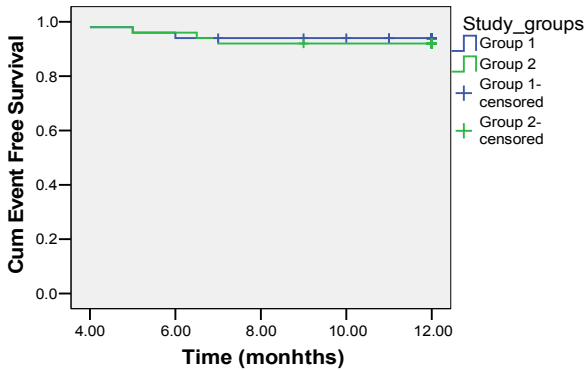
	<b>Group 1 (DES)</b>	<b>Group 2 (CCS)</b>	<b>P value</b>
<b>Coronary artery disease</b>			
LAD	20	22	0.25
LCX	24	17	
RCA	6	11	
<b>Site of lesion</b>			
Proximal:	5	9	0.38
LAD	3	4	
LCX	2	3	
RCA	0	2	
MID:	31	25	
LAD	14	9	
LCX	14	10	
RCA	3	6	
Distal:	14	16	
LAD	3	10	
LCX	8	3	
RCA	3	3	
<b>Type of lesion</b>			
A	36	37	0.60
B	13	13	
C	1	0	
<b>Lesion severity (%)</b>			
Mean	84.5±6.4	81±6.54	0.008
Range	82.67 - 86.32	79.13 - 82.86	
<b>Procedural data</b>			
Lesion length (mm)	12.44±3.81	10.92±3.5	0.04
Reference diameter (mm)	2.83±0.7	2.81±0.1	0.21
Stent diameter (mm)	2.65±0.12	2.63±0.13	0.43
Stent length (mm)	18.54±3.99	17.76±4.25	0.34
Inflation pressure (atm)	14.6±1.16	14.24±1.25	0.13
	<b>Group 1 (DES)</b>	<b>Group 2 (CCS)</b>	<b>P value</b>

LAD= left anterior descending artery, LCX= left circumflex artery, RCA= right coronary artery.

**(Table 6):** Follow up data among the 2 study groups.

	<b>Group 1 (DES)</b>	<b>Group 2 (CCS)</b>	<b>P</b>
<b>MACE</b>	3 (6%)	4 (8%)	1.00
<b>Death</b>	1 (2%)	1 (2%)	0.47
<b>MI</b>	2 (4%)	0 (0%)	0.47
<b>TVR</b>	3 (6%)	3 (6%)	1.00
<b>CABG</b>	2 (4%)	0 (0%)	0.07
<b>ISR</b>	3 (6%)	4 (8%)	0.97
<b>Severity of lesion on 2<sup>nd</sup> angiography (%)</b>			
Mean± SD	84.5±6.4	81±6.54	0.008
Range	82.67 - 86.32	79.13 - 82.86	

Combined MACE + ISR occurred in 3 patients in group 1 (DES) while in 5 patients in group 2 (CCS), ( $p=0.71$ , odds ratio= 0.60, 95% confidence interval = 0.15 - 2.37).



Kaplan Meier curve showing the cumulative event free survival comparing the 2 study groups ( $p=0.70$ ).

#### 4. Discussion

Coronary artery disease (CAD) is one of the most common causes of mortality and morbidity across the world (Shewan & Coats., 2010).

Percutaneous coronary interventions (PCI) are a valuable addition to treatment regimens in modern cardiology (Biondi-Zoccai *et al.*, 2005).

The use of intracoronary metallic stents has improved results over balloon dilatation alone and has become standard care for patients undergoing PCI (Brophy *et al.*, 2003). However, in-stent restenosis, leading to recurrence of symptoms, has been the major drawback of bare metal stents (BMS) (Daemen *et al.*, 2008). Drug-eluting stents (DES) were introduced in an attempt to overcome this problem and, due to the improved effectiveness in preventing restenosis, DES implantation has rapidly grown to up to 80% of cases in some countries (Stettler *et al.*, 2007).

However, recently there have been concerns about their long-term Safety (Bavry *et al.*, 2006), due to an increase in late stent thrombosis, possibly linked to delayed endothelialisation of the stent struts. Delayed endothelial cell growth is due to a non-selective inhibitory action of the drug on targeting both smooth muscle cell proliferation and endothelial cell regeneration (Joner *et al.*, 2006).

Moreover, DES definitely increases the cost of PCI when compared with BMS and debate is ongoing over the long-term cost-effectiveness of these devices (Filion *et al.*, 2009).

The beneficial clinical data on DES are mainly derived from trials comparing DES with first-generation thick-strut stainless steel BMS. However, outcomes can be different between stents depending on material and design (Sangiorgi *et al.*, 2007, Briguori *et al.*, 2002).

Stents with thinner struts have shown less restenosis and less repeated interventions (Kastrati *et al.*, 2001, Pache *et al.*, 2003).

This effect may be due to more rapid re-endothelialisation after deployment of thinner-strut stents, reducing vascular injury and inflammation (Kastrati *et al.*, 2001, Rittersma *et al.*, 2004).

With the progressive development of BMS manufacturing, the use of cobaltchromium alloy has appeared promising. This alloy has shown good biocompatibility and appeared to limit the adverse proliferative response seen with other alloys (Filion *et al.*, 2009, Hoffmann *et al.*, 2002).

In addition, cobalt-chromium compared with stainless steel allows reduction in strut thickness with increased flexibility, conserving both radial strength and deliverability (Kereiakes *et al.*, 2003).

This study was done to determine and compare one year prognosis of 100 enrolled non diabetic patients with stable coronary artery disease for elective PCI in small artery stenosis (< 3.0 mm in diameter and < 25 mm in length), all patients had single vessel disease.

In the present study, the use of drug eluting stent versus cobalt chromium stent was associated with a significant reduction in target vessel revascularization through one year follow-up with no difference in death, nonfatal myocardial infarction and coronary artery bypass graft.

In our study there was a statistically significance difference among both groups regarding hypertension which was more common in group II. In group I and II, hypertension was present in 86% and 54% respectively.

Otherwise, there was no statistically difference between the two groups concerning baseline characteristics including (age, gender, smoking, obesity, dyslipidemia, family history of CAD, angina class, C reactive protein, ejection fraction).

As regarding the baseline angiographic and procedural data there was significant difference between group I and group II according to lesion severity. In group I the lesion severity ranged from 82.67 to 86.32 % with a mean  $84.5 \pm 6.4$ , while in group II the lesion severity ranged from 79.13 to 82.86% with a mean  $81 \pm 6.54$ .

Otherwise, there was no statistically difference between the two groups concerning baseline angiographic and procedural data including (coronary artery disease, site of lesion, type of lesion, reference diameter, stent diameter, stent length and inflation pressure).

As regarding our Primary End Point which was the incidence of MACE (Death, MI, CABG and TVR) for a one year follow up, major adverse cardiac events occurred in group I in three patients (6%). As in group II, four patients (8%) with no statistical significance.

One patient died during follow up period (during GABG) in group I and one patient in group II due to unknown cause with no significant difference.

Two patients developed MI in group I but MI didn't occur in group II which is considered not significant.

TVR occurred in group I in three patients (6%) and in the same number of patients in group II with no statistical significance.

CABG occurred in two patients (4%) in group I, while it didn't occur in group II with no statistical significance.

Instent restenosis occurred in group I in three patients (6%), while in group II four patients (8%) with no statistical significance.

Our results came in agreement with the **ENDEAVOR II** randomized controlled trial to evaluate the long-term clinical and economic outcomes for subjects receiving Endeavor drug-eluting versus Driver bare-metal stents (both Medtronic Cardio Vascular, Santa Rosa, California). From 1,197 subjects randomized to receive Endeavor ( $n = 598$ ) versus Driver ( $n = 599$ ) stents, the use of Endeavor versus Driver reduced a 4-year target vessel revascularization rates per 100 subjects (10.4 vs. 21.5; difference: -11.1; 95% confidence interval [CI]: -16.0 to -6.1;  $p < 0.001$ ), with no difference in the rates per 100 subjects of death (5.0 vs. 5.2; difference: -0.2; 95% CI: -2.7 to 2.4;  $p = 0.90$ ) or nonfatal myocardial infarction (3.2 vs. 4.4; difference: -1.2; 95% CI: -3.4 to 1.0;  $p = 0.29$ ). The ENDEAVOR II trial found a higher incidence of TVR in the cobalt chromium stents group with statistically significant difference between the two groups, due to many factors including that nearly one-third of patients had multivessel CAD and type C lesions. Also 22.2% of patients were diabetic. Finally, most subjects received pre-treatment with balloon angioplasty and increased duration of follow-up period.

While in our study there was low incidence of TVR with no statistically significance difference in both groups due to small number of patients included. All patients were non diabetic and most of them with single and type (A,B) lesions. (**Eric I et al., 2009**).

Also our results are in agreement with the **BASKE Ttrial** (BASel Stent Cost Effectiveness trial) to the fact that it is unknown which patients benefit most from drug-eluting stents (DES) against bare-metal stents (BMS) in a long-term clinical outcome. Data from 826 consecutive patients with angioplasty, randomized 2:1 to DES vs. BMS, with an 18-month follow-up for cardiac death/myocardial infarction (MI) and non-MI-related target-vessel revascularization (TVR) were analyzed for interactions between stent type and patient/vessel characteristics predicting events. Rates of 18-month TVRs were lower with DES vs. BMS use (7.5 vs. 11.6%,  $P = 0.05$ ), but similar for both stents regarding cardiac death/MI (DES, 8.4%; BMS, 7.5%;  $P = 0.70$ ) (**Hans-Peter Brunner-La Rocca et al., 2007**).

Moreover, our results in group II were also in agreement with the clinical and angiographic analysis in **Class Study** which was a prospective, nonrandomized, multicenter study designed to assess the safety and efficacy of a cobalt-chromium alloy-based stent (Driver) in patients with stable or unstable angina pectoris. A total of 203 lesions were treated in 202 enrolled patients. The occurrence of MACE was 4.0%, with TLR accounting for 1.0%, Q wave MI for 0%, non Q wave MI for 2.5% and deaths accounting for 1.5%. This study demonstrated that the Driver cobalt-chromium alloy stent can be used with a low 6-month incidence of major adverse cardiac events, a low 6-month binary restenosis rate, and a high angiographic and procedural success. (**Victor et al., 2006**).

Also our results in group II were in agreement with Christoph et al, who found that in two hundred and three patients (mean age  $67 \pm 12$  years; 63% male) were included in the Registry; 199 patients (98%) were controlled clinically (including noninvasive stress tests) 6 and 12 months after stent implantation. Clinically driven angiographic controls were performed in 37 patients (18.2%) at mean 6 months after stenting. The study demonstrated that stenting of small arteries with **Arthos Pico** is safe and effective in the prevention of major adverse cardiac events during 6- and 12-month follow-up (**Christoph et al., 2007**).

Moreover our results in group II were in agreement with **Coroflex Blue Registry** which is an international, prospective, multicenter registry enrolling patients with symptomatic ischemic heart disease attributable to single de novo or restenotic nonstented lesions of a single vessel amenable for percutaneous stenting. The registry included 2,315 patients (mean age  $64.3 \pm 11.1$  years, 19.8% diabetes, 37.3% acute myocardial infarction). This registry demonstrates the safety and efficacy of the Coroflex Blue cobalt-chromium stent platform in real-world practice. (**Wolfgang et al., 2010**).

Our results are also in agreement with the Vision registry, in which MACE was 6.2%, with TLR accounting for 4.3%, Q wave MI for 0.4%, non Q wave MI for 0.45% and deaths accounting for 1.2%. As for the Driver registry, the MACE was 4% with 3.4% TLR, no other complications were found. (**Kereiakes et al., 2003, Sketch et al., 2005**).

While Mehdi *et al.*, found that 832 deaths occurred over a 4.5-year interval among 8,032 patients. Of these, 6,053 received a DES and 1,983 patients had a BMS. All-cause mortality was significantly lower in unadjusted and adjusted Cox proportional models with DES (hazard ratio: 0.62, 95% confidence interval: 0.53 to 0.73;  $p < 0.001$ ). Similarly, in the propensity-matched group, DES remained associated with lower mortality compared with BMS (adjusted hazard ratio: 0.54, 95% confidence interval: 0.45 to 0.66;  $p < 0.001$ ). This study



revealed that DES was associated with lower mortality in this “real-world” setting (**Mehdi et al., 2008**).

Also Brian et al found the 1-year primary event rate was 15% in the DES group (95% confidence interval [CI]: 11% to 18%), compared with 27% in the BMS group (95% CI: 23% to 31%,  $p < 0.001$ ). A Cox proportional hazard regression model was used to adjust for differences in patient characteristics and showed a 1-year DES hazard ratio of 0.51 (95% CI: 0.36 to 0.71,  $p < 0.001$ ). After 1 year, event rates for the primary outcome increased in DES subjects relative to BMS patients, such that longer follow-up analyses resulted in nonsignificant comparisons. These results suggest that the use of DES for patients with stable coronary disease is superior to BMS for 1 year, but that the increment in benefit decreased over continued follow-up (**Brian et al., 2009**).

In these studies there is an apparent difference in the MACE results in comparison with our lower rates of MACE. This difference is in attribution for three main reasons. First, all our patients are not diabetic and the second is due to small number of patients included. The third is that these studies are comparing DES with conventional bare metal stainless steel stent.

#### Conclusion:

The use of drug eluting stent versus cobalt chromium stent was associated with a significant reduction in target vessel revascularization in small artery stenosis through 1-year follow-up with no difference in death, nonfatal myocardial infarction.

#### References

1. Bavry, A.A., Kumbhanim D.J. & Helton, T.J. (2006). Late thrombosis of drug-eluting stents: A meta-analysis of randomized clinical trials. *American Journal of Medicine*, 119, 1056-1061.
2. Biondi-Zoccai G, Abbate A, Agostoni P, Testa L, Burzotta F, Lotrionte et al. (2005). Long-term benefits of an early invasive management in acute coronary syndromes depend on intra-coronary stenting and aggressive anti-platelet treatment: a meta-regression. *Am Heart J*, 149:504-11.
3. Brian Horst, Charanjit S. Rihal, David R. Holmes, John F. Bresnahan, Abhiram Prasad, Gerald Gau, Ryan Lennon, Amir Lerman, (2009). Comparison of Drug-Eluting and Bare-Metal Stents for Stable Coronary Artery Disease, *J Am Coll Cardiol Intv*, 2:321– 8.
4. Briguori C, Sarais C, Pagnotta P, Liistro F, Montorfano M, Chieffo A, et al. (2002). In-stent restenosis in small coronary arteries: impact of strut thickness. *J Am Coll Cardiol*, 40:403-9.
5. Brophy JM, Belisle P, Joseph L. (2003). Evidence for use of coronary stents: a hierarchical ayesian meta-analysis. *Ann Intern Med*, 138:777-86.
6. Christoph Strehblowa, Mariann Gyo` ngyo` sia, Gerald Zenkerb, Hubert Wallnerc, Matthias Heigertc, Peter Siostrzonekd, Robert Tischlerb, Peter Probst, Irene Langa, Heinz Sochora and Dietmar Glogara. (2007). Small vessel stenting with cobalt–chromium stents (Arthos Pico) in a real world setting. *Coronary Artery Disease*, 18:305–311.
7. Cutlip DE, Chauhan MS, Baim DS, Ho KKL, Popma JJ, Carrozza JP. (2002). Clinical restenosis after coronary stenting: perspectives from multicenter clinical trials. *J Am Coll Cardiol*, 40:2082–9.
8. Daemen J, Boersma E, Flather M, Booth J, Stables R, Rodriguez A, et al. (2008). Long-term safety and efficacy of percutaneous coronary intervention with stenting and coronary artery bypass surgery for multivessel coronary artery disease: a meta-analysis with 5-year patient level data from the ARTS, ERACI-II, MASS-II, and SoS trials. *Circulation*, 118:1146-54.
9. Eric L. Eisenstein, William Wijns, Jean Fajadet, Laura Mauri, Rex Edwards, Patricia A. Cowper, David F. Kong, Kevin J. Anstrom, (2009). Long-Term Clinical and Economic Analysis of the Endeavor Drug-Eluting Stent Versus the Driver Bare-Metal Stent 4-Year Results From the ENDEAVOR II Trial. *J A C C C : C A R D I O V A S C U L A R I N T E R V E N T I O N S*, 2: 1178-87.
10. Filion KB, Roy AM, Baboushkin T, Rinfret S, Eisenberg MJ. (2009). Cost-effectiveness of drug-eluting stents including the economic impact of late stent thrombosis. *Am J Cardiol*, 103:345-9.
11. Fischman, D.L., Leon, M.B. & Baim, D.S. (1994). A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. *Stent Restenosis Study Investigators*. *New England Journal of Medicine*. 331, 496-501.
12. George D. Dangas, Bimmer E. Claessen, (2010). In-Stent Restenosis in the Drug-Eluting Stent. *J Am Coll Cardiol*, 56:1897–907.
13. Hans-Peter Brunner-La Rocca, Christoph Kaiser, and Matthias Pfisterer on behalf of the BASKET Investigators. (2007). Targeted stent use in clinical practice based on evidence from the Basel Stent Cost Effectiveness Trial (BASKET). *European Heart Journal*, 28: 719–725.
14. Hoffmann R, Mintz GS, Haager PK, Bozoglu T, Grube E, Gross M, et al. (2002). Relation of stent design and stent surface material to subsequent in-stent intimal hyperplasia in coronary arteries determined by intravascular ultrasound. *Am J Cardiol.*, 89:1360-4.

15. Hsieh IC, Chien CC, Chang HJ. (2001). Acute and long-term outcomes of stenting in coronary vessel \_ 3.0 mm, 3.0 –2.5 mm, and \_ 2.5 mm.b *Cathet Cardiovasc Intervention*, 53:314–22.
16. Joner M, Finn AV, Farb A, Mont EK, Kolodgie FD, Ladich E, et al. (2006). Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. *J Am Coll Cardiol*, 48:193-202.
17. Kastrati A, Mehilli J, Dirschinger J, Dotzer F, Schunhlen H, Neumann FJ, et al. (2001). Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR STEREO) trial. *Circulation*, 103:2816-21.
18. Kastrati A, Dibra A, Mehilli J. (2006). Predictive factors of restenosis after coronary implantation of sirolimus- or paclitaxel-eluting stents. *Circulation*, 113:2293–300.
19. Kereiakes DJ, Cox DA, Hermiller JB, Midei MG, Bachinsky WB, Nukta ED. (2003). Guidant Multi-Link Vision Stent Registry Investigators. Usefulness of a cobalt chromium coronary stent alloy. *Am J Cardiology*, 92:463:466.
20. Kereiakes DJ, Cox DA, Hermiller JB, Midei MG, Bachinsky WB, Nukta ED. (2003). Guidant Multi-Link Vision Stent Registry Investigators. Usefulness of a cobalt chromium coronary stent alloy. *Am J Cardiology*, 92:463:466.
21. Lloyd-Jones D, Adams R, Carnethon M, De Simone G, Ferguson TB, Flegal K. (2009). Heart disease and stroke statistics—2009 update: a report from the American Heart Association statistics committee and stroke statistics subcommittee. *Circulation*, 119:480–6.
22. Morice MC, Bestehorn HP, Carrie D, Macaya C, Aengevaeren W, Morice MC. (2003). Stenting for small coronary vessels. *J Invasive Cardiology*, 15:3779.
23. Pache J, Kastrati A, Mehilli J, Schühlen H, Dotzer F, Hausleiter J, Fleckenstein M, Neumann F-J, Sattelberger U, Schmitt C, Müller M, Dirschinger J and Schömig A. (2003). Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISARSTEREO- 2) trial. *Journal of the American College of Cardiology*, 41: 1283-1288.
24. Rittersma SZ, de Winter RJ, Koch KT, Bax M, Schotborgh CE, Mulder KJ, et al. (2004). Impact of strut thickness on late luminal loss after coronary artery stent placement. *Am J Cardiol*, 93:477-80.
25. Sangiorgi G, Melzi G, Agostoni P, Cola C, Clementi F, Romitelli P, et al. (2007). Engineering aspects of stents design and their translation into clinical practice. *Ann Ist Super Sanita*, 43:89-100.
26. Shewan LG, Coats AJ. (2010). Ethics in the authorship and publishing of scientific Int *J Cardiology*, 144:1-2.
27. Sketch MH Jr, Ball M, Rutherford B, Popma JJ, Russell C, Kereiakes DJ. (2005). Driver investigators. Evaluation of the Medtronic (Driver) cobalt–chromium alloy coronary stent system. *Am J Cardiology*, 95:8–12.
28. Stettler C, Wandel S, Allemann S, Kastrati A, Morice MC, Schömig A, et al. (2007). Outcomes associated with drug-eluting and bare metal stents: a collaborative network meta-analysis. *Lancet*, 370:937-48.
29. Victor Legrand, Henning Kelbaek, Karl Eugen Hauptmann, Dietmar Glogar, Wolfgang Rutsch, Gilles Grollier, Paul Vermeersch, Joseph Elias, and Cornelis Carolus De Cock, (2006). Clinical and Angiographic Analysis With a Cobalt Alloy Coronary Stent (Driver) in Stable and Unstable Angina Pectoris, *Am J Cardiol*, 97:349 –352.
30. Wolfgang Bocksch, Francisco Pomar, Mieczyslaw Dziarmaga, Damras Tresukosol Omar Ismail, Bronislav Janek Joerg Carlsson, and Jean-Philippe Simon, (2010). Clinical Safety and Efficacy of a Novel Thin-Stru Cobalt–Chromium Coronary Stent System: Results of the real world coroflex blue registry, *Catheterization and Cardiovascular Interventions*, 75:78–85.