INDIAN HEART JOURNAL 66 (2014) 525–529

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/ihj

Original Article

Real world experience with an indigenously manufactured stent Cobal C – A retrospective study

B.K.S. Sastry [a,*], Nirmal Kumar [b], Rajeev Menon [b], Anuj Kapadia [b], C. Sridevi [b], G. Surya Prakash [b], N. Krishna Reddy [b], M. Srinivasa Rao [b]

[a] Consultant Cardiologist, CARE Hospitals, Hyderabad, Telangana, India
[b] CARE Hospitals, Hyderabad, Telangana, India

ARTICLE INFO

Article history:
Received 25 July 2014
Accepted 6 August 2014
Available online 18 September 2014

Keywords:
Bare metal stent
Cobalt chromium stent
Restenosis
Cobalt+C stent

ABSTRACT

Background: Second generation bare metal stents made of cobalt chromium alloy are superior to first generation stain less steel stents. The thin struts are shown to reduce clinical and angiographic adverse outcomes.

Objective: To study the long term clinical and angiographic outcomes in patients who underwent coronary angioplasty with an indigenously made cobalt chromium bare metal stents with thin strut Cobal+C™ (Relisys).

Methods: A total of 268 consecutive patients who underwent coronary angioplasty with Cobal+C stents were studied retrospectively. Clinical follow up was done after a minimum period of nine months through telephonic interview and angiographic follow up was done in 80 patients chosen randomly. The end points analyzed included major adverse cardiac events (MACE) at nine months and the rate of binary restenosis at follow up angiogram done between 9 and 15 months post angioplasty.

Results: Thirty four percent were diabetic and 33% had acute myocardial infarction. Females constituted 17%. Mean stent diameter was 2.88 ± 0.28 and mean stent length 18.8 ± 4.2. MACE at nine months was 4.5% with TLR 0.3%. The rate of binary restenosis was 21%. Patients with longer stent lengths and non-compliance with medications had significantly higher rates of binary restenosis.

Conclusions: The use of Relisys Cobal+C stents was associated with good long term clinical and angiographic outcomes as evidenced by low incidence of MACE and binary restenosis rates for a bare metal stent.

1. Introduction

Despite the overwhelming popularity of drug eluting stents (DES),[1] bare metal stents (BMS) continue to be used in about 30% of patients due to various reasons. The most common reason to use BMS in our country is financial constraints. The clinical and angiographic conditions that are likely to be benefited more by the use of BMS include planned surgical procedure within six months of angioplasty and bleeding disorders which might hamper the treatment with dual

* *Corresponding author*. Tel.: +91 98495 99888.
E-mail address: bkssastry@hotmail.com (B.K.S. Sastry).
http://dx.doi.org/10.1016/j.ihj.2014.08.015

antiplatelet therapy, short discrete lesions and lesions in larger vessels.

Surprisingly the existing publications on cobalt chromium stents are scant. These are mainly prospectively controlled observational studies done in highly selected patient population using limited stent sizes and lengths and angiography done at the end of six months. Some information about their performance can also be obtained from the randomized clinical trials in which these BMS are used as comparator against DES.

In the initial stages of its usage, the major limitation of BMS made of stainless steel was acute stent thrombosis and the high incidence of restenosis.[2–6] The safety and efficacy of stents with thin struts was realized.[7–10] Stents made of cobalt chromium alloy have been specifically developed since it is stronger and denser than stainless steel. These properties make it possible to design stents with thinner struts while maintaining radial strength and also radio opacity. The new designs with thinner struts contributed to lesser vessel damage and faster and complete endothelialization and better outcomes.

Cobal+C is an indigenously developed stent manufactured by Relisys, Mangalpally, Telangana, India. It is a cobalt chromium coronary stent with ultra thin strut thickness –0.0029″ compared to 0.0032″ of Vision stent (Abbott Vascular, Illinois, USA) and 0.0036″ of Driver stents (Medtronic, Minneapolis, USA). It has superior surface smoothness due to a patented and improved electro polishing technology. As shown by the Atomic Force Microscopic study, the Root Mean Square (RMS) surface roughness of the Cobal+C stent is 3.22 nm which is 37% lower than that of Driver stent (5.12 mm) (Data on file in Relisys). It has been in clinical use for the past seven years. We planned to study the long term safety and efficacy of Cobal+C stents in real world situation.

1.1. *Objective*

To study the long term clinical and angiographic outcomes in patients who underwent percutaneous coronary intervention with Cobal+C stents.

2. Methodology

This is a retrospective study conducted in consecutive patients who underwent Cobal+C stent implantation at CARE Hospitals, Banjara Hills and Nampally in Hyderabad from January 2009 to May 2010. Patients in whom stents other than Cobal+C were used in conjunction were not included for the study. This is an all comer study and the indication for the angioplasty procedure and technique of stent implantation were as per the discretion of the treating physician. All patients were advised dual antiplatelet therapy with clopidogrel and aspirin. Patients who were not pre-treated received a bolus dose of 300 mg of clopidogrel and 325 mg soluble aspirin just before the procedure.

Telephonic follow up using structured questionnaires developed for this study was done at a minimum period of 9 months post stent implantation by study coordinators. Angiographic follow up was performed in 80 randomly selected patients. They were invited to have coronary angiogram. Follow up coronary angiogram was done between 9 and 15 months after the index procedure with a median of 12 months. Two of the authors had independently assessed binary restenosis by visual assessment. Inter observer variation was resolved by consensus.

For the purpose of this study, major adverse cardiac events (MACE) was defined as a Composite of cardiac death, myocardial infarction [Q wave and non Q wave (CK-MB > 5 × upper limit of normal)], emergency bypass surgery, or repeat target vessel revascularization (TLR) at 9–15 months post stent implantation. Rate of binary restenosis was defined as the percent of patients with a percent in-stent or in segment diameter stenosis of ≥50% in check angiogram performed at 9–15 months post stent implantation.

2.1. *Statistical analysis*

Continuous variables are reported as means and standard deviations. Categorical variables are reported as numbers (percentages). Statistical analysis was limited to comparisons of groups who had binary restenosis with those who did not. Fischer Exact test was used for categorical variables and two tailed Student's *T*-test was used for continuous variables.

3. Results

Within the study period, a total of 268 patients 182 from CARE hospital, Banjara Hills and 86 from CARE Hospital, Nampally were treated with Cobal+C stents. Among these patients, only 261 could be contacted for follow up assessment while 7 of the total cohort could not be contacted.

3.1. *Baseline characteristics*

The age of patients ranged from 30 to 88 yrs and females were 17%. Thirty one percent were diabetic. Acute MI and unstable angina were the clinical indication for 33% and 61% patients. The baseline demographics are shown in Table 1 and baseline clinical and angiographic profile in Table 2.

3.2. *Angiography and angioplasty details*

Three hundred and fourteen stents were implanted in 283 vessels of 261 patients. Ninety percent of patients had single vessel coronary artery disease. Stent dimensions ranged from 2.5 mm to 3.5 mm in diameter and 10 mm–32 mm in length. The mean stent diameter was 2.88 ± 0.28 and mean stent length 18.8 ± 4.21. Angiographic success was achieved in all patients.

3.3. *Clinical follow up*

Seventeen patients had died after the index procedure of which 11 were due to cardiac causes (4.2%) and six were due to non cardiac causes. Six of the cardiac deaths were in hospital in patients undergoing primary angioplasty for acute myocardial infarction. After discharge two deaths occurred in patients with severe left ventricular dysfunction, while three

Table 1 – Baseline demographics and clinical characteristics.

Total no. of patients	261[a]
Age (range in yrs)	30–88
Female gender	45 (17%)
Diabetes	90 (34%)
Hypertension	135 (52%)
Current smoking	96 (37%)
Previous PCI	None
Previous CABG	1 (0.38%)

CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.
[a] 7 of the total 268 consecutive patients were lost to follow up.

other patients had myocardial infarction and died at home after a period of three months. Further details in these late deaths were not available. One patient had TLR with CABG. Twelve patients had MACE. No patient in this cohort presented to our hospital with sub acute thrombosis or stroke or angina requiring repeat percutaneous coronary intervention. In more than three fourth of the patients who had MACE, acute MI was the clinical indication for angioplasty. Nearly 67% of them were diabetic and two had severe LVD (Table 3).

3.4. *Angiographic follow up*

Follow up angiogram was done in 80 patients (30%) from 9 to 15 months with a median of 12 months following the initial procedure. Of these 80 patients, 26% of patients continued to be active smokers and 30% were not compliant with medications including antiplatelet drugs and statins at the time of follow up (Table 4). Drug compliance was for variable period of

Table 2 – Baseline, clinical and angiographic characteristics.

Clinical indications	
Total number of patients	261[a]
AMI	86 (33%)
Unstable angina	174 (66%)
Stable angina	3 (1%)
Severe LV dysfunction	24 (9%)
Total no. of target vessels	283
Single vessel disease	238 (90%)
Two vessel disease	25 (10%)
Target vessels ($n = 283$)	
LAD	131 (46%)
LCX	39 (14%)
RCA	99 (35%)
OM	12 (4%)
Ramus	1 (0.35%)
LIMA	1 (0.35%)
SVG	1 (0.35%)
Total no. of stents	314
Stent diameter (mean ± SD)	2.88 ± 0.28
Stent length (mean ± SD)	18.8 ± 4.21
Angiographic success	261 (100%)

AMI = Acute myocardial infarction; LV = Left ventricle; LAD = Left anterior descending artery; LCX = Left circumflex artery; RCA = Right coronary artery; OM = Obtuse marginal; LIMA = Left internal mammary artery; SVG = Saphenous vein graft.
[a] 7 of the total 268 consecutive patients were lost to follow up.

Table 3 – Clinical follow up.

MACE	12 (4.5%)
All cause mortality	17 (6.5%)
Death due to cardiac cause	11 (4.2%)
Sub acute thrombosis	0 (0%)
TLR (with CABG)	1 (0.3%)
Repeat PCI of the target vessel	0 (0%)
Non-compliance with medications	33 (12.5%)
Continued smoking	42 (16%)

time. Binary restenosis was found in 17 patients (21%). In this group with restenosis, 71% were not compliant with medications while 41% were diabetic and 35% continued to smoke, all known risk factors for restenosis. The mean stent diameter was significantly less in this group compared to those without restenosis (2.75 ± 0.16 Vs 2.9 ± 0.3 mm $p < 0.03$). Similarly mean stent length was significantly more in this group compared to those without restenosis (21.6 ± 5.6 mm V 18.3 ± 4.2 $p < 0.005$) (Table 5).

4. Discussion

In this retrospective study which reflected the real world situation, indigenously manufactured cobalt chromium stent Cobal+C was comparable to published data with other cobalt chromium stents.

This all comer retrospective study with a median follow up period of 12 months cannot be compared directly with any prospective registry or a randomized controlled trial. There are both positive and negative aspects to this kind of analysis. In a prospective registry structured follow up of patients would lead to better adherence of medication and life style changes like quitting smoking habit. These in turn would lead to better patient outcomes. In a randomized controlled trial patient enrollment is often selective and treatment and follow up are well controlled. The kind of close monitoring itself would affect the outcomes as it is noted that patients in randomized controlled trials tend to have better outcomes than patients in real world situation. Unless it is an all comer trial, the data would not be applicable to all the patients. The retrospective analysis of our patient cohort truly represents real world situation as it exists in our circumstances.

In this cohort, patients with acute myocardial infarction were 33%, stents less than 3 mm diameter were used in 56% of

Table 4 – Baseline characteristics of patients with angiographic follow up.

No of patients who had follow up angiogram	80
Female gender	10 (12.5%)
Current smokers	21 (26.2%)
Non-compliance with medications	24 (30%)
Diabetes mellitus	25 (31.2%)
Systemic hypertension	42 (52.5%)
Indications for angioplasty	
AMI	29 (36.2%)
Unstable angina	49 (61.2%)
Stent diameter (mean ± SD)	3 ± 0.294
Stent length (mean ± SD)	19.07 ± 4.73
Binary restenosis	17 (21.2%)

Table 5 – Comparison of clinical, angiographic and procedural characteristics of patients with and without binary restenosis.

	With binary stenosis ($n = 17$) Total no. of stents = 21	Without binary stenosis ($n = 63$) Total no. of stents = 71	p Value
Indications for PCI			
Acute MI	6 (35.2%)	24 (34%)	NS
Unstable angina	11 (64.7%)	38 (54%)	NS
Risk factors			
Diabetes mellitus	7 (41%)	18 (25%)	NS
Hypertension	9 (52.9%)	33 (46%)	NS
Active smoking	6 (35.2%)	15 (21%)	NS
Drug non-compliance	12 (70.5%)	12 (17%)	0.0001
Stent diameter in mm (mean ± SD)	2.75 ± 0.16	2.9 ± 0.3	0.03
Stent length in mm (mean ± SD)	21.6 ± 5.6	18.3 ± 4.2	0.0051

patients and stents with length ≥20 mm were used in 37%, 16% of patients continued to smoke and 13% pf patients stopped all medication. All these factors would adversely affect the clinical outcomes and restenosis rates.[11–13] Even then, the observed results are good for a bare metal stent. It can be assumed that the clinical and angiographic outcomes would have been even better if we had used stringent clinical, angiographic inclusion and exclusion criteria, and used only stents with certain dimensions and followed these patients prospectively ensuring adherence to medication and life style changes as done in published clinical trials of other BMS.

The MACE rate of 4.5% and lower TLR rate of 0.3% are comparable to other published reports of cobalt chromium stents. In prospective studies MACE at six months ranged from 5.7% to 10.6% and TLR from 3.4% to 9.8%.[14–17] Higher mortality and lower TLR in our study reflect the kind of patient population that included 37% with acute myocardial infarction undergoing primary angioplasty.

Binary restenosis rate was 21% at an average of 12 months, and it compares well with other cobalt chromium stents. In Endeavor II trial the reported binary restenosis rate at the end of 8 months in Driver stent arm was 35%.[18] Patients with acute MI were not included in these studies. Moreover, the results were of eight months post angioplasty compared to median time of 12 months for angiography in our study. In other trials done using Driver stent ≥3 mm in diameter the six month angiograohic restenosis rates varied from 15 to 26% in select patients.[19] More than 50% of our patients had <3.0 mm stents implanted which correlates strongly with restenosis. It is interesting to note that with Driver stents, the TLR at six months was 3.4% whereas; at nine months it almost doubled.[19]

In a prospective real world study involving Asian population using Coroflex stent the binary restenosis rate was 47.5% at six months.[15] Though the study involved complex lesions and acute MI patients and stents smaller than 3.0 mm were used like in our study, it had excluded lesion lengths of >25 mm. In our study, stent sizes of length >24 mm constituted 18% and this subset with longer stent length has higher restenosis rates.

The cobalt chromium Vision and Minivision stent study which included real-world population like our study had shown comparable restenosis rates. The restenosis rate at six months with Vision and Minivision stents were 17.9% and 45.5% respectively. Together, the restenosis rate was 30%.[20]

Poor compliance with medication is a well known phenomenon in the developing countries and 13% percent of our total cohort had discontinued anti-platelets which is unlikely in any other prospective study. Among the patients with binary restenosis 71% stopped antiplatelet agents. This difference was found to be significant when compared with patients who did not have binary restenosis. Physicians have to be vigilant about this and caution their patients accordingly. This kind of adversely influencing data was not looked into/or reported in other published studies using other cobalt chromium stents.

There are certain limitations to this study. Besides being a non-randomized and retrospective study, it was done from only two centres and angiographic core lab analysis was not done. It cannot be commented if similar results will be reproduced in a multi centre study. Lesion characteristics influence the outcomes of procedures but, they were not studied. The safety and efficacy of this stent in treating lesions in LMCA and coronary bypass grafts could not be ascertained as there was only one patient in each of these.

It may be concluded that though this is not a head to head comparative study with other stents, Cobal+C™ stent was found to have good long term clinical and angiographic outcomes. This is in spite of presence of multiple adversely influencing factors. Direct comparative studies will give better data.

Conflicts of interest

All authors have none to declare.

REFERENCES

1. Silber S, Albertsson P, Avile's FF, et al. Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. Guidelines for percutaneous coronary interventions. The task force for percutaneous coronary interventions of the European society of cardiology. *Eur Heart J*. 2005;26:804–847.
2. Hirshfeld Jr JW, Schwartz JS, Jugo R, et al. The M Heart Investigators. Restenosis after coronary angioplasty: a multivariate statistical model to relate lesion and procedure variables to restenosis. *J Am Coll Cardiol*. 1991;18:647–656.

3. Arjomand H, Turi Zoltan G, McCormick Daniel, Goldberg Sheldon. Percutaneous coronary intervention: historical perspectives, current status, and future directions. *Am Heart J*. 2003;146:787–796.
4. Elezi S, Kastrati A, Pache J, et al. Diabetes mellitus and the clinical and angiographic outcome after coronary stent placement. *J Am Coll Cardiol*. 1998;32:1866–1873.
5. Hoffmann R, Mintz GS. Coronary in-stent restenosis — predictors, treatment and prevention. *Eur Heart J*. 2000;21:1739–1749.
6. Daemen J, Boersma E, Flather M, et al. Long-term safety and efficacy of percutaneuous 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*. 2008;118:1146–1154.
7. Kastrati A, Dirschinger J, Boekstegers P, et al. Influence of stent design on 1-year outcome after coronary stent placement: a randomized comparison of five stent types in 1,147 unselected patients. *Catheter Cardiovasc Interv*. 2000;50:290–297.
8. Pache J, Kastrati A, Mehilli J, et al. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO-2) trial. *J Am Coll Cardiol*. 2003;41:1283–1288.
9. Briguori C, Sarais C, Pagnotta P, et al. In-stent restenosis in small coronary arteries: impact of strut thickness. *J Am Coll Cardiol*. 2002;40:403–409.
10. Kastrati A, Mehilli J, Dirschinger J, et al. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO Trial). *Circulation*. 2001;103:2816–3282.
11. Kastrati A, Schomig A, Elezi S, et al. Predictive factors of restenosis after coronary stent placement. *J Am Coll Cardiol*. 1997;30:1428–1436.
12. Chen Yung-Lung, Yip Hon-Kan, Chen Chien-Jen, et al. Predictors of 6-month angiographic restenosis inside bare-metal stent in Chinese patients with coronary artery disease. *Acta Cardiol Sin*. 2009;25:1–6.
13. Mercado Nestor, Boersma Eric, Wijns William, et al. Clinical and quantitative coronary angiographic predictors of coronary restenosis. *J Am Coll Cardiol*. 2001;38:645–652.
14. Visconti Gabriella, Focaccio Amelia, Tavano Davide, Airoldi Flavio, Briguori Carlo. The CID chrono cobalt–chromium alloy carbofilm-coated coronary stent system. *Int J Cardiol*. 2010;10:1016.
15. Bocksch Wolfgang, Pomar Francisco, Dziarmaga Mieczyslaw, et al. On behalf of the coroflex blue registry investigators. *Catheter Cardiovasc Interv*. 2010;75:78–85.
16. Xu Ya-Wei, Wei Yi-Dong, Tang Kai, et al. Multi-link Vision and Minivision stent registry in Asian patients with coronary artery disease: a prospective, multi-center study. *Chin Med J*. 2007;120:1093–1096.
17. Sketch Michael H, Ball Michael, Rutherford Barry, Popma Jeffrey J, Russell Catherine, Kereiakes Dean J, On behalf of the Driver Investigators. Evaluation of the Medtronic (Driver) cobalt-chromium alloy coronary stent system. *Am J Cardiol*. 2005;95:8–12.
18. Fajadet J, Wijns W, Laarman GJ, et al, ENDEAVOR II Investigators. Randomized, double-blind, multicenter study of the Endeavor zotarolimus-eluting phosphorylcholine-encapsulated stent for treatment of native coronary artery lesions: clinical and angiographic results of the ENDEAVOR II trial. *Circulation*. 2006;114:798–806.
19. http://www.accessdata.fda.gov/cdrh_docs/pdf3. *Medtronic Driver Rapid Exchange*. Accessed 13.06.14.
20. Wöhrle J, Nusser T, Hoffmann S, Kochs M. Angiographic results of the cobalt chromium vision and mini-vision stents. *Can J Cardiol*. 2009;25:581–584.