



Original Article

One-year clinical outcome of percutaneous coronary intervention with very long (≥ 40 mm) drug-eluting stent



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ABSTRACT

Objectives: The aim of this study was to assess the clinical outcome of patients with diffuse coronary lesions treated with very long drug-eluting coronary stents (DES) (≥ 40 mm) over a period of one year. **Methods:** This single-center prospective study enrolled a total of 343 consecutive patients (376 long stents) who underwent percutaneous coronary stent implantation with very long DES. One year clinical outcomes were analyzed. A subgroup analysis of diabetic patients was also performed.

Results: One year follow up data was available for 314 patients (91.5%). All-cause mortality was 5 (1.6%). Eleven (3.5%) patients had non-ST-elevation myocardial infarction. Definite / probable stent thrombosis was reported in 7 (2.2%) patients. Over one year, 3 (1%) patients underwent target lesion revascularization (TLR). The total number of target lesion failure was 9 (2.9%). The rate of target lesion failure at one year was 2.6% using one vessel per patient analysis. Two patients had ischemic stroke. Any major adverse cardiac event (MACE) was observed in 19 (6%) patients. The event rates between sirolimus and everolimus stent groups were compared - cardiac death (1.7% vs 1.5%; $p = 0.911$), stent thrombosis (2.5% vs 1.7%; $p = 0.612$), TLR (1% vs 0.8%; $p = 0.878$), any MACE (7% vs 4.1%; $p = 0.284$). Exertional dyspnea was reported by 47 (15%) patients at the end of one year. Dual antiplatelet adherence rate was 96% ($n = 301$ of 314).

Conclusion: Use of very long stents (≥ 40 mm) for diffuse coronary lesions is safe and effective with acceptably low event rates. No significant differences in event rates were observed between the types of DES used in this study (Sirolimus Vs. everolimus).

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What is already known

Use of longer stents to treat diffuse coronary lesions results in better outcomes compared to use of multiple overlapping stents. The safety and efficacy of 38 mm DES has been established.

What this study adds

Use of very long drug-eluting stents measuring 40 mm and above to treat diffuse coronary lesions is safe and effective with acceptably low event rates. This might prove to be a cost-effective strategy to treat long lesions.

1. Introduction

Drug-eluting stents (DES) have been found to be efficacious and cost-effective in complex coronary disease subgroups such as long

lesions.^{1,2} However, complex lesions often involve the use of multiple, overlapping stents. This led to greater periprocedural complications including myocardial ischemia,³ stent fracture,^{4,5} and late stent thrombosis. As compared with using a single longer stent, use of multiple stents leads to impaired vascular healing,⁶ leading to complications. Recently, studies have shown promising results with newer generation DES when used in an overlapping manner.^{7,8} There is data on “full metal jacket” or “vessel reconstruction” for diffuse coronary lesions. However, not only the total stented length but also the overlapped segments predispose to adverse events. Hence, the advantages of stenting long lesions with fewer long stents still remain valid. The use of longer stents for full lesion coverage is the preferred strategy for percutaneous coronary intervention (PCI) to reduce the incidence of restenosis in long lesions. Very long DES (≥ 40 mm) can cover diffuse coronary lesions, thereby reducing the number of stents needed. To date, however, no study has reported data regarding the use, safety, and efficacy of such long stents. The aim of the present study was to assess the clinical outcome of patients with diffuse coronary lesions treated with very long coronary stents measuring at least 40 mm over a period of one year.

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2. Methods

2.1. Study population

The study included 343 consecutive patients who underwent coronary stent implantation with at least one DES of length 40 mm and above at a tertiary care academic hospital in south India between March 2015 and March 2016. Patients who underwent primary percutaneous coronary angioplasty (PTCA) with long stents were excluded from the study. The baseline characteristics of all patients included in the study were obtained from the hospital PTCA registry. The baseline characteristics assessed included age, sex, presence or absence of co-morbidities like diabetes mellitus, hypertension, dyslipidemia, smoking status, previous myocardial infarction (MI), indication for PTCA (stable coronary artery disease, unstable angina pectoris, post-MI). Diabetes was diagnosed if fasting blood sugar >126 mg/dl or random blood sugar >200 mg/dl or on diabetic medications. Hypertension was diagnosed if systolic blood pressure (BP) of ≥ 140 mmHg and/or diastolic BP of ≥ 90 mmHg or on antihypertensives. The left ventricular (LV) function was assessed by two-dimensional (2D) echocardiography using Simpson's method. LV dysfunction was defined as an ejection fraction (EF) <50%. Lesion and procedure characteristics include the extent of coronary artery disease (single/double/triple vessel disease), lesion location, lesion length, preprocedural stenosis and periprocedural complications.

2.2. Stenting procedures and antiplatelet therapy

Stent implantation procedure was performed according to current standard techniques. The lesions were prepared by adequate predilatation in all cases. All stents were post dilated with noncompliant balloon, and stent deployment was assessed with stent boost imaging in two orthogonal planes. Intravascular ultrasound (IVUS) or optical coherence tomography imaging was not performed during stenting procedure. During the procedure, patients received intravenous weight-adjusted heparin treatment to achieve an activated clotting time of >300 s. The use of glycoprotein IIb/IIIa inhibitors was at the discretion of treating physician. All patients were given a loading dose of 300 mg aspirin and 300 mg clopidogrel before PTCA. After the procedure, 150 mg aspirin daily was continued indefinitely in all patients. The prescription of at least 12 months of clopidogrel 75 mg daily was recommended for all patients, irrespective of stent type. The duration of further extended clopidogrel use was determined at the physician's discretion.

2.3. Study end points and definitions

The primary outcome of the study was a composite of (i) All-cause mortality and (ii) Non-fatal target vessel MI. The secondary outcomes were (i) Major adverse cardiac events (MACE) (ii) Target vessel MI (iii) Target vessel revascularization (TVR) and (iv) Target lesion revascularization (TLR). All deaths were considered to be of cardiac cause unless a noncardiac cause could be identified. A diagnosis of MI was based on the presence of new Q waves in at least two contiguous leads on an ECG or an elevation of troponin I concentration above the normal upper limit in at least two blood samples. Revascularization of the target-lesion and vessel was considered ischemia-driven if there was $\geq 50\%$ stenosis of the diameter of the treated lesion or vessel, as well as ischemic signs (i.e., positive functional tests) or symptoms, or a target vessel (or lesion) diameter stenosis $\geq 70\%$ with or without documented ischemia. Stent thrombosis was defined as definite or probable by academic research consortium definitions. Target lesion failure (TLF) was a composite of cardiac death, target vessel MI, or

clinically driven TLR. MACE was defined as a composite of death, any acute coronary syndrome (ACS), emergent or clinically driven repeat TLR. Lesion success was defined as <50% residual stenosis of the target lesion in final angiogram. Procedure success was defined as <50% residual stenosis of the target lesion and no in-hospital MACE.

2.4. Clinical follow-up

All the patients included in the study were followed up every three months for one year. Patients were followed up either during outpatient visits or by telephonic interview. One year follow up of the patients were completed by March 2017. The functional status and the outcome events were recorded including target vessel MI, TVR, hospitalization with ACS, heart failure. The target vessel was identified by electrocardiographic localization / coronary angiogram (CAG). Patients who had residual or new onset ischemic symptoms underwent either treadmill test or CAG based on the clinical profile.

2.5. Statistical analysis

From the previous studies⁹ with an estimated mortality of 1% and non-fatal MI of 4% and 2.5% precision, the sample size was estimated to be 300. Statistical analysis was performed using SPSS 17.0 (IBM, New York, U.S). Continuous variables are presented as mean \pm standard deviation and are compared with Student's *t*-test or Mann-Whitney U test. Categorical variables are presented as frequencies or percentages and are compared with chi-square or Fisher exact test *t*-tests, as appropriate. A *p* value of <0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics and procedural results

A total of 343 patients were included in the study. The baseline characteristics of the patients are given in Table 1. Lesion characteristics are given in Table 2. The study population included 261 males (76%) and 82 females (24%). The mean age of the study population was 56.75 ± 8.76 years. About 46% (*n* = 158) of the patients were diabetics, 54% (185) were hypertensives, and 14% were active smokers. Previous ST elevation MI (STEMI) was documented in 51% (*n* = 175) of the patients. The indication for PTCA was non-ST elevation MI (NSTEMI) in 99 patients (29%) and chronic stable angina in 113 patients (33%). LV dysfunction was observed in 55 (16%) patients. About 43% (*n* = 149) of the patients had single vessel disease, 37% (*n* = 128) had two vessel disease and 17% (*n* = 61) had three-vessel disease. A total of 376 long stents were implanted in the study population. In 236 patients, at least one short stent (<40 mm) was implanted in addition to the long stent. In 58 of these patients, the short stent was implanted in the same vessel as the long stent (overlapping the long stent in 31

Table 1
Baseline characteristics of the study population (*n* = 343).

S.no	Characteristics	No (%)
1.	Males	261 (76)
2.	Mean age	56.75 ± 8.76
3.	Diabetes mellitus	158 (46)
4.	Hypertension	185 (54)
5.	Active smokers	16 (5)
6.	Previous STEMI	175 (51)
7.	Chronic stable angina	99 (29)
8.	NSTEMACS	113 (33)
9.	LV dysfunction	55 (16%)

Table 2

Lesion and procedure characteristics (n = 343).

S.no	Characteristics	No (%)
1.	Single vessel disease	149 (43%)
2.	Two vessel disease	128 (37%)
3.	Three-vessel disease	61 (17%)
4.	Left main stenting	8 (2.5%)
5.	Stented vessel - LAD	129 (38%)
6.	Stented vessel - RCA	173 (51%)
7.	Chronic total occlusion	93 (27%)
8.	Sirolimus DES	247 (62%)
9.	Everolimus DES	151 (38%)
10.	Lesion success	376 (100%)
11.	Procedural success	98%
12.	Periprocedural complication	6 (1.7)
13.	Mean diameter of long stents implanted (mm)	3.12 ± 0.77
14.	Mean no. of long stents per patient	1.09 ± 0.30
15.	Mean length of stented segment (mm)	41.63 ± 2.77

patients). The artery most frequently stented with a long stent was right coronary artery followed by left anterior descending artery. In 8 (2.5%) patients the PTCA involved stenting the left main coronary artery. The most frequently used stent length was 40 mm, implanted in 70% of the study patients. Forty four (13%) patients were stented with a 44 mm stent while 42 (12%) patients had a 48 mm stent. Overall, 27% (n=93) of the long stents were implanted in chronic totally occluded lesions. The mean number of long stents implanted per patient was 1.09 ± 0.30. The mean length of the stented segment was 41.63 ± 2.77 mm. The mean size of the long stents used was 3.12 ± 0.77 mm. In total, 62% (n = 233) of the DES used were sirolimus-eluting, and 38% (n = 143) were everolimus eluting stents. The sirolimus eluting coronary stent systems employed in the study include Biomime aura (Meril life sciences, Gujarat, India) in 31%; Genx Sync (MIV therapeutics Ltd, Surat, India) in 16%; Orsiro (Biotronik AG, Bülach, Switzerland) in 9%; Yukon choice flex (Translumina therapeutics, New Delhi, India) in 6%. The everolimus eluting stents used in the study were Eternia (Innovolution Healthcare Pvt. Ltd., New Delhi, India) in 18%; Enovo (Veritas Bioventions Pvt. Ltd, Gujarat, India) in 13%; Xience Xpedition (Abbott Vascular, Illinois, USA) in 1%

3.2. Procedural and clinical outcomes

The rate of lesion success was 100%. Procedural success was achieved in 98% (n = 337 of 343). Periprocedural events include intraprocedural pulmonary edema in 2 and coronary perforation in 2 patients. There was one event of extensive coronary dissection and 3 cases of major side branch occlusion with ischemic ECG changes and periprocedural elevation of cardiac enzymes (creatinine kinase-MB levels >5 times upper normal levels).

One year follow up data was available for 314 patients (91.5%) obtained by in-person evaluation in 216 (69%) patients, and by telephonic interview in 98 (31%) patients. The follow up data was not available for 29 patients. A total of 346 long stents were implanted in these 314 patients. One year outcomes are given in Table 3. All-cause mortality was 5 (1.6%). Two patients died within the first month of the procedure. Two other patients died at 5th and 6th months post-procedure. One patient died ten months after the procedure. Of these, three patients had NSTEMI, and two patients had sudden cardiac death (first and fifth month post procedure). Three of these patients had sirolimus-eluting, and two had everolimus eluting stents. All three patients with possible late stent thrombosis were compliant to dual antiplatelet therapy. Eleven (3.5%) patients had NSTEMI during follow up. Of these, seven had been treated with sirolimus-eluting stent, and four had everolimus eluting stent. Two (0.6%) patients had target vessel STEMI (first and third months post procedure). The total stent

Table 3

One year clinical outcomes (n = 314).

S.no	Outcomes	No (%)
1.	All-cause mortality	5 (1.6)
2.	Cardiac death	5 (1.6)
3.	Target lesion failure	9 (2.9)
4.	Target vessel MI	2 (0.6)
5.	Target lesion revascularisation	3 (1)
6.	Clinically driven target vessel revascularization	3 (1)
7.	NSTEMACS	11 (3.5)
8.	Stroke	2 (0.6)
9.	Heart failure	1 (0.3)
10.	Total probable stent thrombosis	7 (2.2)
11.	Probable late stent thrombosis	3 (1)
11.	Any MACE	19 (6)
12.	CAG on follow up	14 (4.4)
13.	Drug compliance	98%

thrombosis rate was 2.2% (7 patients). One patient (0.3%) had definite stent thrombosis, three patients (0.9%) had probable and three patients (0.9%) had possible stent thrombosis. A total of 17 (5.4%) patients underwent CAG on follow up, of which nine patients had patent stents, 4 had mild ISR, 3 (1%) patients underwent TVR (first, fourth and fifth months post procedure), and 1 had total occlusion of the long stent in which an attempt to revascularize failed. The total number of target lesion failure was 9 (2.9%). Two patients had ischemic stroke. Any MACE was observed in 19 (6%) patients. The time plot of cumulative incidence of one-year outcomes is shown in Fig. 1. No statistically significant difference in outcomes was observed between the groups treated with sirolimus or everolimus eluting stents (Table 4). Drug compliance rate was 98%. Dual antiplatelet adherence rate was 96% (n = 301 of 314). Subgroup analysis of diabetic patients did not show a significant difference in primary or secondary end points compared to those without diabetes (Fig. 2).

4. Discussion

This study was a prospective evaluation of the safety and efficacy of very long DES. Despite majority of the study patients having multivessel disease, the use of long stents resulted in a low TLF rate (2.6%). The rate of definite or probable stent thrombosis was also low, indicating that the use of long stents was safe through 1-year follow-up. Despite the fact that a substantial proportion of the study patients were diabetic, rates of clinical and safety events were low. The rates of TLF and its component end points at 1-year follow-up in our study were low. The percutaneous

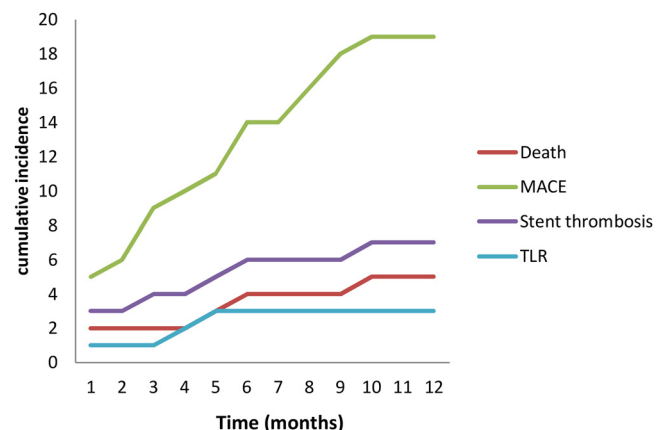
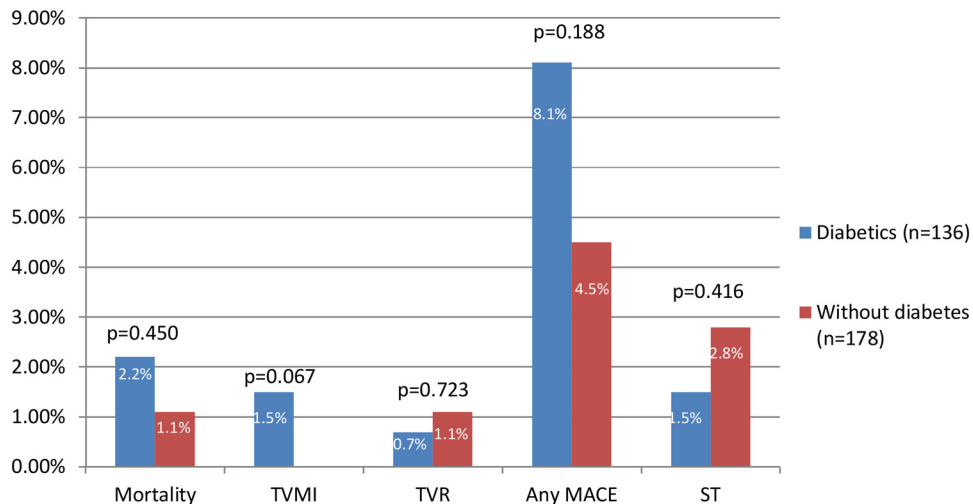
**Fig. 1.** Cumulative incidence of outcomes over a period of 12 months.

Table 4

Comparison of one year clinical outcomes between patients treated with sirolimus or everolimus eluting stents.

S.No	Outcomes	SES (n = 201) [no (%)]	EES (n = 121) [no (%)]	P value
1.	Cardiac death	3 (1.7)	2 (1.5)	0.911
2.	TLR	2 (1)	1 (0.8)	0.878
3.	Stent thrombosis (definite/probable)	5 (2.5)	2 (1.7)	0.612
4.	NSTEMI	7 (3.5)	4 (3.3)	0.932
5.	Target vessel STEMI	2 (1.0)	0	0.169
6.	Any MACE	14 (7)	5 (4.1)	0.284

**Fig. 2.** Comparison of one year outcomes between patients with and without diabetes.

treatment of long native coronary lesions with drug-eluting stent-IV Trial (LONG-DES-IV)¹⁰ specifically studied only long lesions (defined as ≥ 25 mm). The study employed 38-mm R-ZES and 1-year TLF rate was 14.0%. Most events were non-Q-wave target vessel MI (n = 29 of 36). The low rates of stent thrombosis, cardiac death, and target vessel MI in our study confirm the safety of the use of ≥ 40 mm stents through 1 year. There were only three early probable stent thrombosis events. It is assumed that the procedure related factors are more often the cause of early stent thrombosis rather than device-related factors¹¹. Moreover, the rate of definite or probable stent thrombosis (2.2%) in our study is comparable to that of Resolute All Comers¹² (2.3%), and the rate of late stent thrombosis in our study (1%) was comparable to the results of RESOLUTE International¹³ (0.9%). The rate of total stent thrombosis (2.2%) in our study is higher than that reported (0.8%) in the sirolimus arm of LONG-DES IV trial. This could be due to various reasons – the long lesion was defined as ≥ 25 mm; the mean lesion length in the sirolimus arm was 31.0 ± 13.5 mm; the mean stented length is different in the two studies; the use of intraprocedural IVUS in 82% of the patients. The composite rate of cardiac death and target vessel MI was 2.2% at one year (n = 7 of 314), with five cardiac deaths and two non-fatal target vessel MI events. The rates of cardiac death (1.6%) in our study were consistent with Resolute All Comers (1.3%) and RESOLUTE International (1.4%) trials. A post-hoc analysis of this study found no differences in clinical outcomes between patients with and without diabetes. This study was not powered to assess such differences, so these results may be considered exploratory.

Two other studies evaluated 1-year follow-up of 38-mm stent (X-EES)^{14,15} and (P-EES).^{16,17} Patients in the X-EES study were implanted with either 33- or 38-mm stent, and in the P-EES study either a 32- or 38-mm stent was used. All patients in our study were implanted with a stent length of at least 40 mm. Both these

studies had a smaller sample size (X-EES: n = 104 and P-EES: n = 102) than our study (n = 314). The TLF rate for P-EES was 3.1% which was comparable to our result (2.6%)

5. Study limitations

The study has several limitations. This was a non-randomized single-center study involving a small number of patients. The study population was heterogeneous with respect to the DES implanted. Majority of the patients were treated with sirolimus-eluting stents. The events of NSTEMI (n = 11) cannot be entirely attributed to long stents since 9 of these patients, in addition, also had shorter stents in other vessels. Also, CAG was not performed in all patients with NSTEMI which otherwise might have led to target vessel revascularization and thereby influenced the results. Since the event rates were low, the loss of follow up data of 9% of the patients might have affected the results.

6. Conclusions

The present study demonstrated that the use of very long stents (≥ 40 mm) for diffuse coronary lesions is safe and effective with acceptably low event rates. This strategy of treating diffuse coronary lesions might prove cost-effective, without affecting the procedural success rate. Further, no significant difference in event rates was observed between the types of DES used in our study (Sirolimus Vs. everolimus) over a period of one-year follow-up.

Conflict of interest

None

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