Study of safety and efficacy of novel Sirolimus-Eluting Stent incorporating properties of Drug Coating Balloon among real world patients focusing among younger population (under 35 years)

Recommended Citation

Study of Safety and Efficacy of Novel Sirolimus-Eluting Stent Incorporating Properties of Drug Coating Balloon Among Real World Patients Focusing Younger Population (<35 years)

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Abstract

Objective: Aim of study was to evaluate safety and efficacy of abluminal Mitigator DES + Sirolimus Eluting Stent (Envision Scientific, Surat, India) incorporating novel technology of fusion coating of bioresorbable polymer on both abluminal surface of stent and exposed parts of balloon among real world patients specially focusing younger patients (<35 years).

Method: 1293 patients received Mitigator DES + at LPS Institute of Cardiology, Kanpur, India. Primary outcome was target lesion failure (TLF)- composite of cardiovascular death, target vessel myocardial infarction (TVMI), and target lesion revascularization (TLR) and secondary end points including peri-procedural device failure (failure of stent delivery, change of stent, stent fracture), target vessel failure (TVF), and patient oriented composite end point (POCE)- composite of all deaths, MI, and revascularization and stent thrombosis (ST) at 1-year follow-up.

Result: Younger population comprised of 374 (29%) patients. Various indications of interventions were STEMI (n = 614; 47.4%), NSTEMI (n = 416; 32.2%), UA (n = 161; 12.5%), and CCS (n = 102; 7.9%). TLF at 1 year in young and overall population were 3.4% and 3.5% respectively which was driven by TVMI and TLR in 1.3% and 1.1% patients respectively. POCE was observed in 9.5% in each group mainly contributed by any revascularization (3.9%). Device failure was significantly lower in young group than overall population (1.3% vs. 2.2%; p = 0.04) which was mainly driven by stent delivery (1.1%) and edge dissection (0.5%). Definite and probable ST was 1.3% and 1.7% respectively which was not significant. Young patients showed insignificantly lower TLF, TVF, ST and POCE and significantly lower device failure (1.3% vs. 2.6%; p = 0.04) when compared to patients >35 years. On multivariate regression analysis, complex lesion, in-stent restenosis, failure of stent delivery and edge dissection were independent predictors of events or device success rate.

Conclusion: Mitigator DES+™ is safe among real world patients, including young population.

Keywords: Drug-eluting stent, Target lesion failure, Patient oriented composite end point, Stent thrombosis, Percutaneous coronary intervention

1. Introduction

With the improvement in hardwares and availability of imaging modalities like intravascular ultrasound and optical coherence tomography, PCI is frequently being performed of diffuse, calcified and other complex lesions. Earlier generation of DES were shorter in length and had thicker struts (120 μm), thus making them less trackable and deliverable across the lesion which were subsequently replaced by stents having

thinner stent strut with biodegradable polymer [1]. Compared to the previous generation of drug eluting stent (DES), the current one have shown to provide a better efficacy/safety profile in the treatment of simple as well as complex coronary disease by means of percutaneous coronary angioplasty (PCI). Nevertheless, those proved results are still suboptimal for specific subset of high-risk patients, particularly for diabetic patients and those having small vessel involvement as they are associated with worse outcomes following PCI. The design of typical DES consists of metallic platform and drug polymer (biodegradable/biostable). Durable polymer is associated with very late stent thrombosis, delayed arterial healing and neoatherosclerosis. Restenosis rate is higher among diabetic patients especially those having diffuse and long lesions affecting small vessel (≤ 2.75 mm) [2,3]. These are quite common among Indian population where small vessel affliction is seen in nearly 30%—50% of patients with coronary artery disease. It spurred the introduction of new generations of DES which were theoretically able to circumvent these issue. The primary objective was to assess efficacy and safety of Mitigator DES + Sirolimus eluting stents (Envision Scientific, Surat, India) among real world patients including younger patients (<35 years) as they have different clinico—angiographic profile compared with older population (>35 years). With its unique features it might provide better short as well as long-term outcomes among these subset of population as they constitute significant proportion in India.

2. Material and method

2.1. Study design and participants

This was a prospective and observational study conducted between July 2017 and October 2018 at LPS Institute of Cardiology, Kanpur, India among all comer patients who received Mitigator DES+. Revascularization was based on current guideline. Patients presenting with acute coronary syndrome and chronic coronary syndrome who were refractory to optimal medical treatment were included. Patients younger than <18 years, pregnant women, intolerance to aspirin, P2Y12 inhibitor (clopidogrel, ticagrelor, prasugrel) or sirolimus, anticipated major surgery within 6-months following PCI, life expectancy <12 months, and having cardiogenic shock were excluded.

Baseline demographics of patients and procedural detail including angiographic findings were recorded. They were categorized as young group (<35 years) and old group (>35 years). Lesion was

Abbreviations	
PCI	Percutaneous coronary intervention
DES	Drug eluting stent
DEB	drug eluting balloon
DAPT	Dual antiplatelet
ACS	Acute coronary syndrome
CCS	Chronic coronary syndrome
MI	Myocardial infarction
TLF	Target lesion failure
TVMI	Target vessel myocardial infarction
TLR	Target lesion revascularization
TVR	Target vessel revascularization
ST	Stent thrombosis
POCE	Patient-oriented composite endpoint
ARC	Academic Research Consortium
CAD	Coronary artery disease

classified as type A, B1/B2, C [1]. Procedures were performed after obtaining signed informed consent from all patients. The study was conducted in accordance with Declaration of Helsinki and protocol was approved by institutional ethical committee.

2.2. Study device description

Mitigator DES belongs to Abluminous family of stents consisting of device platform and drug product. Device platform is made from L-605 cobalt chromium alloy having opposite alignment connector having open cells in mid segment and closed cells at both ends imparts it a hybrid design. Peak to peak strut alignment facilitates adequate scaffolding which reduces plaque prolapse and ensures optimal metal to artery ratio. Drug product is combination of sirolimus and biodegradable polymer. It has unique and only technology available among all contemporary DES i.e *fusion coating* (coating on *abluminal surface* of *stent* as well as *exposed parts of balloon*) by which it offers dual advantage of DES as well as DEB (Fig. 1). It ensures homogeneous drug delivery, faster re-endothelialisation while additional 0.5 mm coating at both edges helps to prevent edge restenosis. It elutes 50% sirolimus within one week and 66% within 7-weeks. Polymer completely degrades over 6 months [4].

2.3. Procedure

PCI was performed following standard technique using unfractionated heparin as anticoagulant on weight based dosing (70—100 U/kg). All patients were pre-treated with aspirin and P2Y12 inhibitor and DAPT was continued for at least 1-year followed by aspirin monotherapy indefinitely. Minimum stent inflation time while deployment was
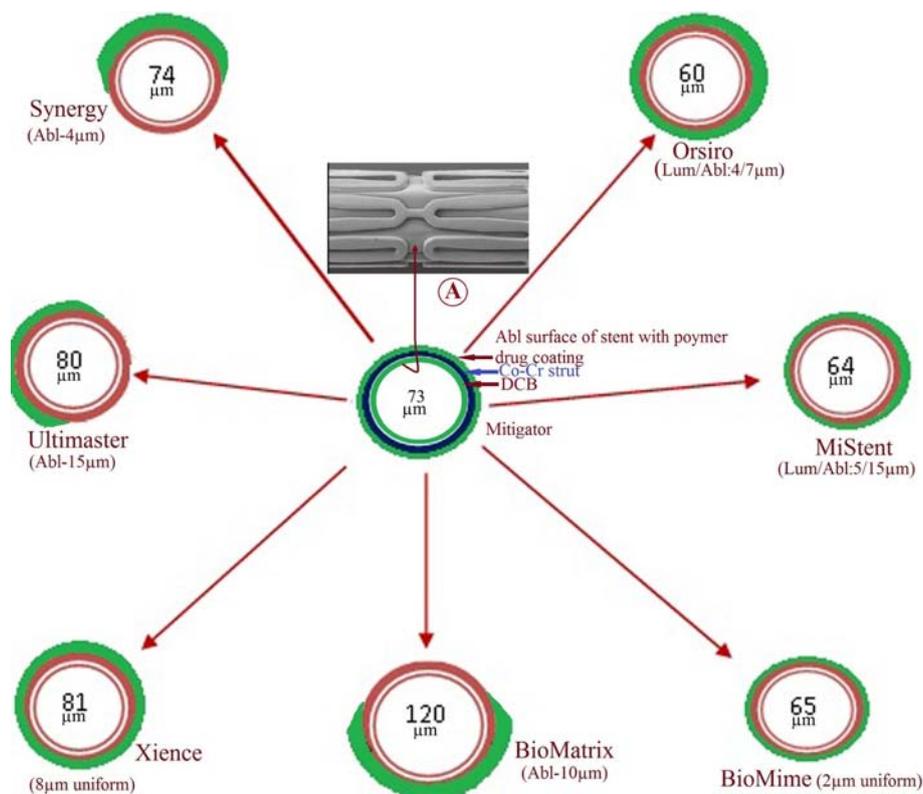
Fig. 1. Schematic representation of strut and polymer thickness of contemporary stents (green colour indicates thickness of polymer; Lum-luminal, Abl-Abluminal; A represents Mitigator DES).

kept 30 s to attain proper conformation of stent and uniform drug-polymer coating across the lesion [5]. Cardiac biomarkers (CK-MB, troponin- I) were measured within 8-h following PCI to diagnose periprocedural MI. Patients were followed clinically at 1 week, 1,3,6,9 and 12 months.

2.4. Study endpoints

Primary endpoint was TLF at 12 months which was composite of cardiac death, TVMI, and ischemia driven TLR. Secondary endpoints included any death, any revascularization, ischemia-driven TVR, ST, periprocedural and spontaneous MI, and *device failure* (composite of failure of stent delivery, change of stent, and stent fracture). POCE was defined as composite of all-cause death, any MI, and any revascularization. ST, periprocedural, and spontaneous MI were defined according to academic research consortium criteria [6]. Target vessel-related MI was attributed to either target vessel or could not be related to another vessel on basis of clinical, ECG, echocardiographic, and angiographic findings. Device success was defined as successful trackibility, delivery and deployment of stent at target lesion with final residual stenosis ≤30%.

2.5. Statistical evaluation

Statistical analyses were performed using SPSS 19.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were expressed as number and percentages and were compared using Pearson's χ^2 test or Fisher's Exact Test. Continuous variables were described as mean ± SD and compared using *t*-test or Mann−Whitney Test as appropriate. Survival analyses and time-to-event outcomes were performed graphically with Kaplan Meier Curve, and mathematically with the log-rank test. P value of ≤0.05 was considered as statistically significance.

3. Results

3.1. Baseline demographics and clinical presentation (Table 1)

Nearly 4500 patients underwent revascularization during index period of which 1293 patients received Mitigator of which 1196 (92.3%) patients completed follow up (Fig. 2). However, type of stent selection was left to operator discretion and on site availability. There was no particular selection bias for this stent as this was an observational study among all comer

Table 1. Baseline demographics and clinical presentation of patients (N = 1293).

Variables	Total patients n (%)	Young Group (≤35 yrs) n (%)	Not Young Group (≥35 yrs) n (%)	P value
N	1293	374	919	
Age (years)	51.1 ± 17.5	32.2 ± 3.2	58.4 ± 10.3	
Male	1027 (79%)	333 (89%)	694 (76%)	0.04
Female	276 (21%)	41 (11%)	225 (24%)	0.03
Serum creatinine (mg/dL)	1.2 ± 0.6	1.1 ± 0.3	1.3 ± 0.7	0.4
CAD risk factors				
Hypertension	303 (23.4%)	44 (11.8%)	259 (28.2%)	0.03
Diabetes mellitus	357 (27.4%)	96 (25.7%)	261 (28.4%)	0.6
Smokers	281 (21.6%)	131 (35.2%)	150 (16.3%)	0.05
Family history of CAD	45 (3.3%)	21 (5.6%)	24 (2.6%)	0.05
Dyslipidemia	330 (25.8%)	83 (22.2%)	247 (26.9%)	0.03
Post CABG	44 (2.2%)	04 (1.1%)	40 (4.3%)	0.03
Clinical Presentation				
STEMI	614 (47.4%)	247 (66%)	367 (39.9%)	0.03
NSTEMI	416 (32.2%)	71 (18.9%)	345 (37.5%)	0.04
UA	161 (12.5%)	37 (9.8%)	124 (13.4%)	0.04
CCS	102 (7.9%)	19 (5.1%)	83 (9%)	0.03
LVEF (%)				
a. >55	78 (6.1%)	21 (5.6%)	57 (6.2%)	0.2
a. 45-55	887 (68.5%)	254 (67%)	78 (68.9%)	0.4
b. 35-45	172 (13.3%)	60 (16%)	112 (12.2%)	0.4
c. <35	156 (12.1%)	39 (10.4%)	117 (12.7%)	0.5
Medications				
Tenecteplase	209 (16.1%)	79 (21.1%)	130 (14.1%)	0.2
Streptokinase	96 (7.4%)	29 (7.7%)	67 (7.3%)	0.6
Aspirin	1275 (98.6%)	371 (99.1%)	904 (98.4%)	0.8
Ticagrelor	885 (68.5%)	259 (69.2%)	626 (68.1%)	0.7
Prasugrel	204 (15.7%)	60 (16%)	144 (15.7%)	0.3
Clopidogrel	206 (15.9%)	53 (14.2%)	153 (16.6%)	0.4
Statin	1257 (97.2%)	368 (98.4%)	889 (96.7%)	0.4
Beta-blocker	960 (74.3%)	280 (75%)	680 (73.3%)	0.6
ACEI/ARB	1062 (82.1%)	311 (83.2%)	751 (81.7%)	0.6
CCB	173 (13.3%)	44 (11.8%)	129 (14%)	0.5
Aldosterone antagonist	202 (15.6%)	57 (15.2%)	145 (15.7%)	0.2
Angiographic severity				
1. SVD	919 (71.1%)	289 (77.3%)	630 (68.6%)	0.04
2. DVD	237 (18.3%)	57 (15.2%)	180 (19.5%)	0.05
3. TVD	137 (9.6%)	28 (7.5%)	109 (11.9%)	0.02
Location of target vessel				
a. LMCA	77 (5.9%)	19 (5.1%)	58 (6.3%)	0.6
b. LAD	635 (49.2%)	230 (61.5%)	570 (62.3%)	0.7
c. LCx	184 (14.3%)	87 (23.2%)	270 (29.3%)	0.5
d. RCA	369 (28.5%)	147 (39.3%)	395 (42.9%)	0.4
e. SVG- OM	12 (0.9%)	00 (00%)	12 (1.3%)	0.02
f. SVG-PDA	16 (1.2%)	04 (1.1%)	12 (1.3%)	0.02

CAD- Coronary artery disease; DM- Diabetes mellitus; CABG- Coronary artery bypass graft; PCI-Percutaneous Coronary Intervention; STEMI-ST Segment Elevation Myocardial Infarction; NSTEMI-Non ST Segment Elevation Myocardial Infarction; UA-Unstable Angina; CCS- Chronic Coronary Syndrome; LVEF- Left ventricular ejection fraction; ACEI- Angiotensin-converting enzyme inhibitor; ARB-Angiotensin-receptor blocker; CCB- Calcium-channel blocker; SVD-Single vessel disease; DVD- Double-vessel disease; TVD- Triple-vessel disease; LAD- Left anterior descending coronary artery; LCx- Left circumflex coronary artery; RCA- Right coronary artery; SVG-Saphenous vein graft; OM- Obtuse marginal branch; PDA- Posterior descending artery.

patients. They were analyzed according to young (<35 years) and older adult (>35 years). Younger group had significantly higher proportion of male patients, smoking, family history of premature CAD while lesser proportion of female, hypertension, dyslipidemia, and CABG. STEMI was significantly higher in them with while NSTEMI, UA, and CCS were significantly less. On angiogram, they had significantly higher number of SVD while DVD, TVD and graft vessel involvement were less.

3.2. Procedural details (Table 2)

Older adults had significantly higher number of complex lesion, CTO, bifurcation lesion, calcified lesion, and in-stent restenosis than younger group.
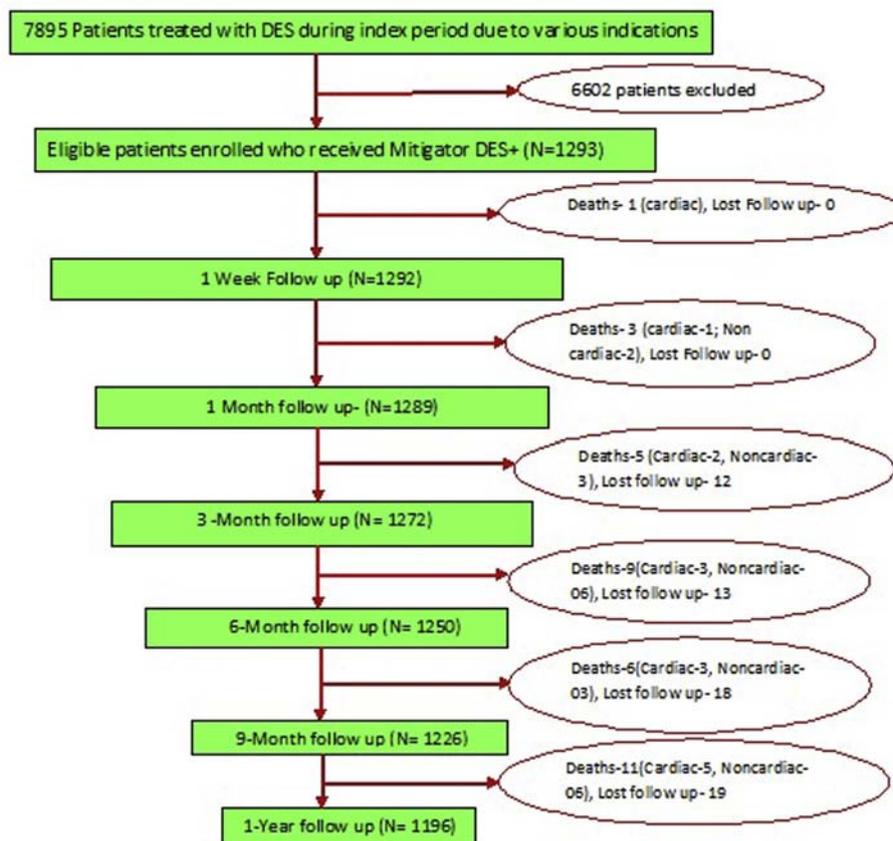
Fig. 2. Flow chart of all patients enrolled in the study (N = 1293).

They also had significantly more number of lesions, and stents per patient.

3.3. Clinical outcomes (Table 3)

TLF was observed in 46(3.5%) among total subjects with non significant intergroup difference though TVMI, TLR, and TVR were relatively lower among younger group (Fig. 3). Stent failure was significantly higher in older group because of failure to deliver the stent at target lesion. TVF and POCE were observed in 60(4.6%) and 124(9.5%) of patients respectively with non significant intergroup difference. On multivariate regression analysis, complex lesion, ISR, failure of stent delivery and edge dissection were independent predictors of events or device success rate (Table 4). Definite and probable ST was observed among 13(1%) and 10(0.8%) patients in overall population with non significant intergroup difference (Fig. 4). Late ST (44%) accounted for majority of stent thrombosis. Figure 5 illustrates Kaplan−Meier survival curves of total patients over 12 month period and outcome was better in younger group than older group (Fig. 6). Of all deaths (n = 35; 2.75%), non-cardiac conditions

(eg, stroke, malignancy, renal failure, sepsis, and pneumonia) attributed for 20(1.6%) deaths while cardiac deaths 15(1.1%) were attributed to ST (n = 3; 20%), heart failure (n = 5; 33%), MI (n = 4; 26%), and arrhythmias (n = 3; 20%).

4. Discussion

Age cut-off for ''young population'' in context of premature CAD is variable (< 35 to < 55 years) due to lack of universally accepted cut-off [7]. Although incidence of MI in younger population may appear relatively low, 20% of subjects younger than 35 years had an unexpectedly high prevalence of CHD [8]. Angiographic findings too differ between group < 35 years and > 35 years. Based on these findings, we decided to choose < 35 years as cut-off as burden of this relatively young population is large in India.

Younger population in India has higher predilection for CAD because of dyslipidemia (high triglyceride, low HDL and normal or slightly raised LDL), diabetes, metabolic syndrome, smoking and stressful lifestyle. Need of repeat revascularisation (50% at 4.7 years) is relatively higher among younger population because of longer expected survival [9,10].

Table 2. *Procedural characteristics of patients (N = 1293).*

Variables	Total patients (N = 1293)	Young Group <35 yrs (N = 374)	Not Young Group <35 yrs (N = 919)	P value
Transfemoral Intervention	1004 (77.4%)	279 (74.6%)	819 (78.9%)	0.4
Transradial Intervention	289 (22.6%)	95 (25%)	194 (21%)	0.5
Size of vessel				0.5
a. 2.25–2.5	211 (16.3%)	57 (15.3%)	154 (16.8%)	
b. 2.5–3	250 (19.3%)	76 (20.3%)	174 (18.9%)	
c. 3–3.5	571 (44.2%)	160 (42.8%)	411 (44.7%)	
d. 3.5–4	208 (16.1%)	64 (17.1%)	144 (15.7%)	
e. > 4	53 (4.1%)	17 (4.5%)	36 (3.9%)	
Lesion characteristics				
a. At least 1 complex lesion	862 (66.7%)	134 (35.8%)	728 (79.1%)	0.04
b. At least 1 bifurcation lesion	132 (10.2%)	29 (7.8%)	103 (11.2%)	0.03
c. At least 1 CTO	171 (13.2%)	26 (6.9%)	136 (14.8%)	0.04
d. At least 1 ostial lesion	59 (4.5%)	17 (4.5%)	42 (4.5%)	0.5
e. At least 1 calcified lesion	57 (4.2%)	11 (2.9%)	46 (5%)	0.02
f. In-stent restenosis (ISR)	29 (2.2%)	05 (1.3%)	24 (2.6%)	0.02
Lesions per patient	1.5 ± 0.2	1.4 ± 0.3	1.7 ± 0.4	0.03
Lesion length (mm)	29 (8–46)	21 (12–36)	32 (12–46)	0.04
Lesion Modification				
a. Direct Stenting	166 (12.9%)	44 (11.7%)	96 (10.4%)	0.6
b. Semicompliant balloon	1064 (82.3%)	317 (84.4%)	768 (83.6%)	0.8
c. Cutting Balloon	63 (4.8%)	13 (3.4%)	55 (5.9%)	0.04
Stent Delivery				
a. Unassisted	1198 (92.7%)	353 (94.4%)	845 (91.9%)	0.05
b. Buddy Wire	54 (4.1%)	11 (2.9%)	43 (4.6%)	0.05
c. GuideZilla mother-in-child system	41 (3.2%)	07 (1.8%)	34 (3.6%)	0.04
Median Stent length per patient (mm)	28 ± 16	23 ± 10	32 ± 12	0.03
Full Metal Jacketing (≥60 mm)	99 (7.7%)	23 (6.1%)	76 (8.3%)	0.4
Stent diameter (mm)	2.7 ± 0.3	2.9 ± 0.5	2.8 ± 0.4	0.5
Thrombosuction	93 (7.2%)	29 (7.8%)	64 (6.9%)	0.5
GP IIb/IIIa inhibitor	172 (13.3)	39 (10.4%)	133 (14.4%)	0.4
Implantation of assigned stents only	1278 (98.8%)	371 (99.1%)	907 (98.6%)	0.5

CTO- Chronic total occlusion; GP- Glycoprotein.

The key findings in our study were: (a) Mitigator DES + is safe and effective among real world patients with acceptable level of clinical event rate (TLF = 3.5%; definite ST = 1%) over 12-month follow-up, (b) rate of CV death, TVMI, and TLR were 1.3%, 1.1%, and 1.1% respectively and (c) outcomes were consistent across pre-specified groups (≤ 35 years and ≥ 35 years).

Male population outnumbered female in our study as there is a gender bias both in diagnosis, presentation and mortality. It also showed rural urban trend as well where proportion of female is even lesser in rural area [8,11].

Our findings were not only concordant but slightly better than reported by Meliga et al. [12]. In their study, young people were considered < 40 years and only small proportion of them had received DES and potent antiplatelets. These were also consistent with event rates reported using relatively thinner DES (Fig. 1) such as Orsiro SES, Synergy EES, Resolute ZES [1], Ultimaster [13] and Biomatrix [14] which reported as 6.7%, 7.5%, 8.3%, 3.4% and 9.2% respectively. The unique design

could have been reason for reduced distal micro-embolism and slow-flow which are associated with adverse outcome. When individual components were analysed, outcome was better among younger group compared to older in term of cardiac death and TLR because of lesser complexities of lesion, CTO and lower median length of stents.

Device success (97.8%) was superior to current generation stents like Supralimus Cruise (97.6%) [15], FIREHAWK (92.4%), Xience (94.8%) [16]. Stent failure was noted in only 1.1% of patients. Compared to older group, younger group fared significantly better because of lesser number of complex lesions, CTO, calcified lesion and shorter stent length. Longer and calcified lesions were major hinderence to stent delivery. As far as primary outcome, POCE, TVF and other end point was concerned, periprocedural outcome was not included in these and hence, had no influence on statistical evaluation. Moreover, our study demonstrated that trackability and deliverability might be an issue among complex lesion like any other DES. Our findings were concordant with findings from

Table 3. *Peri-procedural end point and clinical events during 1-year follow-up (N = 1293).*

Variables	Overall Patients (N = 1293)	Young (<35 years)- (N = 374)	Not Young (>35 years)- (N = 919)	P value
Target Lesion Failure (TLF)	46 (3.5%)	13 (3.4%)	33 (3.5%)	0.8
a. Target vessel MI	18 (1.3%)	05 (1.3%)	13 (1.4%)	0.4
b. Ischemia-driven TLR	13 (1.1%)	04 (1.1%)	09 (1%)	0.5
c. Cardiac death	15 (1.1%)	04 (1.1%)	11 (1.1%)	0.8
Device Failure (Secondary)	29 (2.2%)	05 (1.3%)	24 (2.6%)	0.04
a. Failure of stent delivery	15 (1.1%)	03 (0.8%)	12 (1.3%)	0.02
b. Edge Dissection	07 (0.5%)	01 (0.2%)	06 (0.6%)	0.05
c. Stent fracture	02 (0.1%)	01 (0.2%)	01 (0.1%)	0.6
d. Coronary perforation	02 (0.1%)	01 (0.2%)	01 (0.1%)	0.7
e. Stent dislodgement	03 (0.2%)	01 (0.2%)	02 (0.2%)	0.5
Target Vessel Failure (TVF)	60 (4.6%)	17 (4.5%)	43 (4.6%)	0.5
POCE	124 (9.5%)	36 (9.5%)	88 (9.6%)	0.7
All cause death	35 (2.7%)	10 (2.6%)	25 (2.7%)	0.7
Periprocedural MI	14 (1.1%)	03 (0.8)	11 (1.2%)	0.8
Any MI	38 (2.9%)	11 (2.8%)	27 (2.2.9%)	0.7
Any revascularization	51 (3.9%)	13 (3.5%)	38 (3.8%)	0.6
Ischemia-driven TVR	27 (2.1%)	06 (1.6%)	21 (2.3%)	0.04
Definite stent thrombosis	13 (1%)	03 (0.8%)	10 (1.1%)	0.6
a. Acute (0−1 days)	05 (0.4%)	02 (0.5%)	03 (0.3%)	
b. Sub-acute (2−30 days)	06 (0.5%)	01 (0.2%)	05 (0.5%)	
c. Late (31−360 days)	02 (0.2%)	00 (00%)	02 (0.2%)	
Probable ST	10 (0.8%)	02 (0.5%)	08 (0.8%)	0.5
a. Acute (0−1 days)	02 (0.2%)	00 (00%)	02 (0.2%)	
b. Sub-acute (2−30 days)	04 (0.4%)	01 (0.3%)	03 (0.3%)	
c. Late (31−360 days)	04 (0.4%)	01 (0.2%)	03 (0.3%)	
Definite and Probable ST	23 (1.7%)	05 (1.3%)	18 (1.9%)	0.5
a. Acute (0−1 days)	07 (0.5%)	02 (0.5%)	05 (0.5%)	
b. Sub-acute (2−30 days)	10 (0.8%)	02 (0.5%)	08 (0.8%)	
c. Late (31−360 days)	06 (0.5%)	01 (02%)	05 (0.5%)	

MI- Myocardial infarction; TLR- Target lesion revascularization; TVF-Target vessel failure (composite of cardiac death, target vessel MI, and ischemia-driven TVR); POCE- Patient-oriented composite endpoint (composite of all-cause death, any MI, and any revascularization); ST- Stent thrombosis; TVR- Target vessel revascularization.
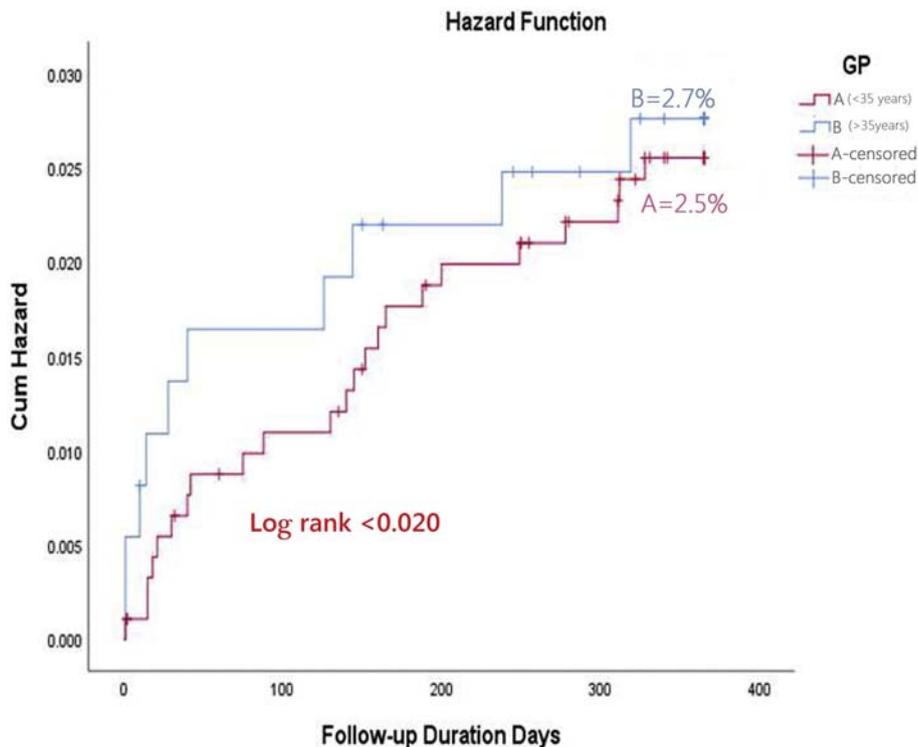

Fig. 3. *TLF over 12 months period of follow up between both group (A<35 years; B > 35 years).*

Table 4. *Predictors of events or device success rate at 12-months by multivariate regression analysis (N = 1293).*

Variables	Odds Ratio (95% CI)	*P*-Value
Age	1.2 (0.8−3.1)	0.6
Long lesion	3.4 (2.1−8.4)	0.05
CTO	3.8 (2.3−7.9)	0.040
Median Stent length	2.6 (0.9−4.3)	0.05
Calcified lesion	6.1 (2.4−15.4)	0.002
In stent Restenosis	3.1 (1.9−5.2)	0.04
Failure of stent delivery	3.3 (2.1−5.7)	0.04
Edge Dissection	2.5 (1.3−4.8)	0.06

TALENT trial [16] in which delivery failure was also considered as outcome but had no interfence on primary as well as secondary outcome. As far as sample size was concerned, indeed it was not very large but at least sufficient enough to draw a reasonable conclusion. These factors support its periprocedural safety regarding implantation.

TVF in our study (4.6%) was better than Orsiro (8.5%), Synergy (8.8%), and Resolute Integrity (10%) [1], Ultimater (7.4%) [13], Supraflex Cruise (5.4%) [15], Firehawk (9.9%), Xience (9.6%) [16], and Biomatrix [17]. Synergy, Orsiro, Biomatrix and Ultimaster stents have similar design in term of abluminal coating except novel fusion coating (Fig. 1). Trend was similar (4.5%) among younger group which proved its safety.

POCE in our study (9.5%) was consistant with results using Orsiro [1], Biomatrix (9.2%) [2], Ultimaster (10.7%) [13], Supralimus Cruize (9.9%) [15],

FIREHAWK (19.3%), and Xience (17.8%) [16]. It was remarkable despite higher proportion of complex lesion, transfemoral intervention, CTO, and longer mean length of stent. It was little higher than result using sirolimus eluting stent (3.9%) by Youn et al., [18] because of higher proportion of transradial intervention (79.1% vs. 22.6%) and lower proportion of CTO (4.2% vs. 13.2%) compared to our study.

Stent thrombosis in our study was little higher (1.7%) compared Orsiro (1.1%), Synergy (1.1%), and Resolute Integrity (0.9%) [1], Ultimater (1.1%) [13], and Supraflex Cruise (1.1%) [19] but similar to FIREHAWK (1.7%) and lower than Xience (2.1%) [16] and Biomatrix (2.4%). [17] Possible reasons could be higher proportion of diabetes, small reference vessel diameter, longer stent length, impaired left ventricular function, and small mean stent diameter in our study. Although no significant intergroup difference were noted (1.3% vs. 1.9%), trend favoured younger group as ST was lower in comparison to contempory stents. Possible reasons for lower rate of late ST could be reduced long-term inflammation as biodegradable polymer minimizes polymer volume.

Diffuse disease, CTO, and multiple lesions sometimes may result into full metal jacketing (FMJ) of vessel (total length of stents in single vessel $\geq$ 60 mm) [19]. In their study of patients with FMJ by Lee et al., TLF and ST were observed in 7% and 1.2% respectively [19]. Similar observations were noted in our study among patients who had
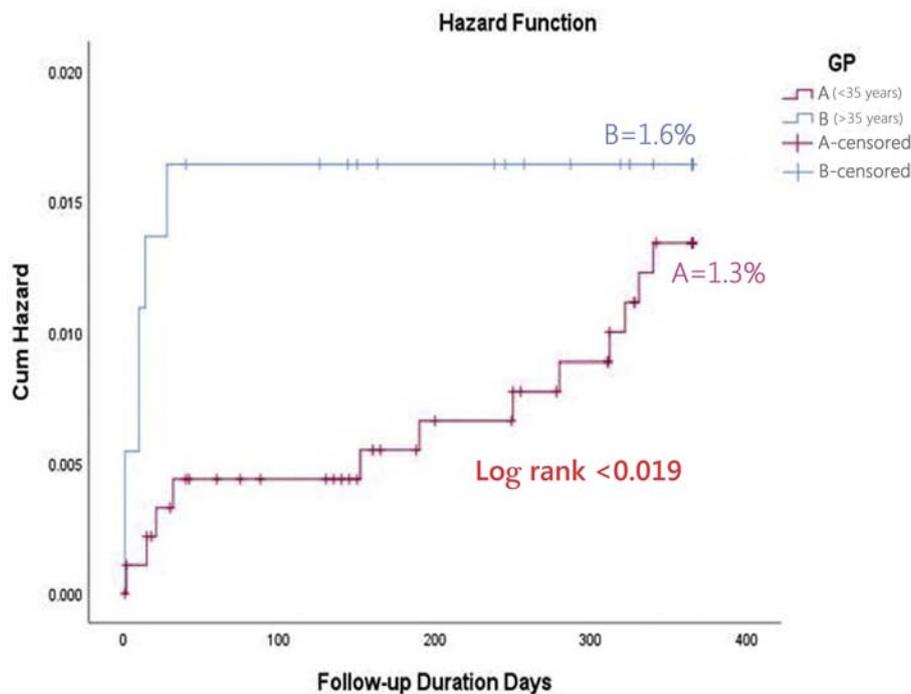

Fig. 4. *ST over 12 months period of follow up between both group (A<35 years; B > 35 years).*
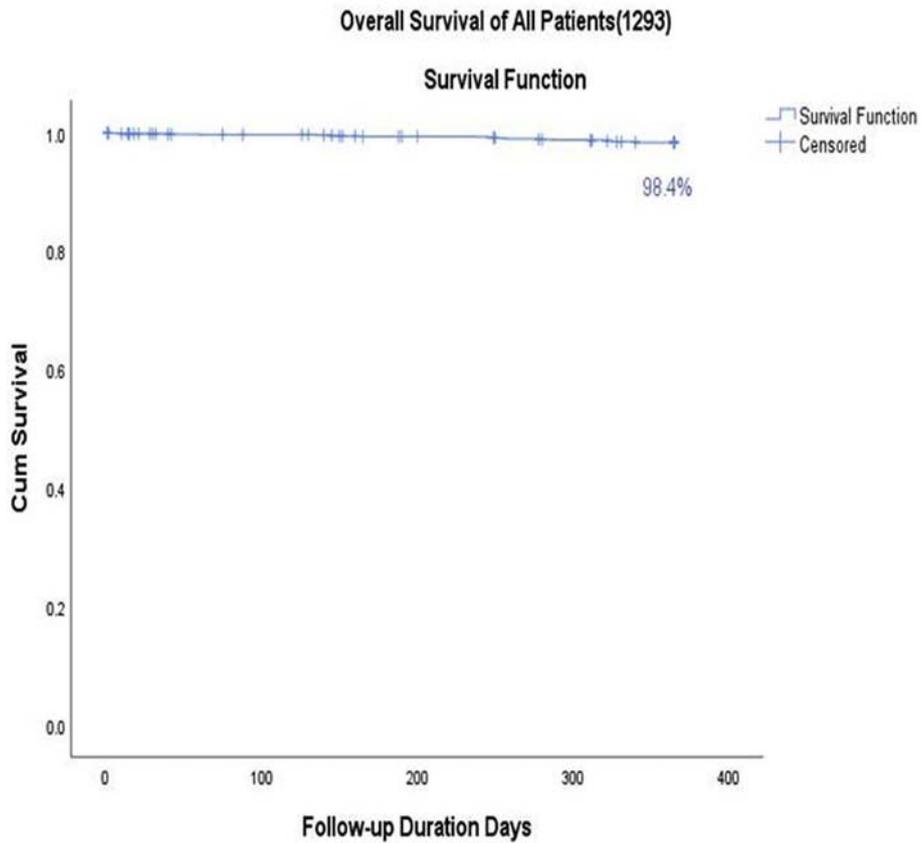
Fig. 5. Kaplan−Meier survival curves of all patients over 12 months period of follow up.
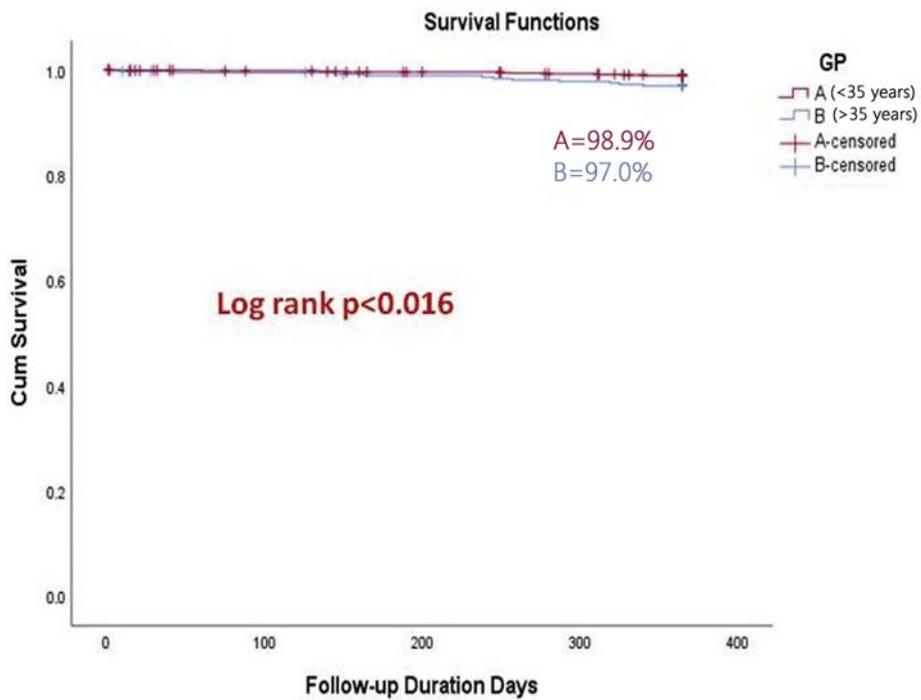

Fig. 6. Kaplan−Meier survival curves of patients over 12 months period of follow up between both group (A<35 years; B > 35 years).

FMJ with no intergroup difference which showed safety of Mitigator in this subgroup.

Incidence of in-stent restenosis (ISR) varies from 5—10% as a result of neointimal proliferation and neoatherosclerosis [20]. DES was found to be the most effective strategy for treating ISR in a meta-analysis which compared conventional balloon angioplasty, bare metal stents, DEB, brachytherapy, rotablation, and DES (sirolimus, paclitaxel, everolimus) because of lower risk of restenosis and need of repeat revascularization [2,3]. In our study, 2.2% patients had ISR (significantly higher in older age group) but their outcome was comparable which indicated safety of Mitigator among this subgroup. Fusion coating might have contributing factor leading to uniform drug delivery across the lesion and beyond.

In current generation stents, polymer-drug coating is applied abluminally, luminally or uniformly on both side (Fig. 1). Vascular smooth muscle cells which grow in response to balloon/stent induced injury are relatively resistant to sirolimus especially in diabetic patients [4,5]. Mitigator stent ensures relatively higher and uniform concentration of sirolimus which lowers restenosis and TLF in this subgroup. Acute gain in minimum luminal diameter is compensated by late luminal loss (0.05—0.10 mm) as result of recoil and intimal hyperplasia [5]. Because of ultrathin design and biodegradable polymer, late luminal loss does not impact significantly on these smaller vessels and in fact potential benefit of these ultrathin-strut stents are most pronounced in such vessels [21].

5. Conclusion

With availability of with longer stent ($\geq$ 40 mm), lower rate of TLF and repeat revascularization, younger patients (< 35 years) can achieve complete revascularization especially those with diabetes and diffuse vessel disease.

6. Limitation

It was observational study with small sample size. Moreover, patients with life expectancy < 12 months and those presenting with cardiogenic shock were excluded. Imaging modalities like IVUS and OCT were not performed. Long term follow up (> 5 years) would have provided further safety data. It was an all comer study among real world patients which typically negated potential drawback of randomized control study.

Author contribution

Conception and design of Study: Santosh Kumar Sinh, Umeshwar Pandey, Mahmodullah Razi, Puneet Aggarwal, Mohit Sachan. Literature review: Santosh Kumar Sinh, Umeshwar Pandey, Mahmodullah Razi. Acquisition of data: Santosh Kumar Sinh, Umeshwar Pandey, Mahmodullah Razi, Mohit Sachan. Analysis and interpretation of data: Santosh Kumar Sinh, Umeshwar Pandey, Awadesh Kumar Sharma, Praveen Shukla. Research investigation and analysis: Awadesh Kumar Sharma, Puneet Aggarwal, Praveen Shukla. Data collection: Awadesh Kumar Sharma, Puneet Aggarwal, Ramesh Thakur. Drafting of manuscript: Mohit Sachan, Praveen Shukla. Revising and editing the manuscript critically for important intellectual contents: Praveen Shukla, Ramesh Thakur. Supervision of the research: Ramesh Thakur.

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Conflict of interest

The authors certify that there is no conflict of interest with any financial organization regarding material discussed in the manuscript.

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