Original Article

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Assessment of Outcomes after Implantation of Bioabsorbable Stents at Long term Follow up in Indian Patients

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Abstract

Background: Bioresorbable drug-eluting vascular scaffolds were developed to overcome the limitations of metallic drug eluting stents. Several studies have shown the non inferiority of the bioresorbable vascular scaffold (Absorb, Abott Vascular) compared to metallic DES with added advantages of stent resorption. However recent studies have reported higher rates of major adverse cardiac events and scaffold thrombosis in patients receiving Absorb bioresorbable vascular scaffold. The product has been withdrawn by the manufacturers since 14 september 2017 in view of 'low commercial sales' and 'safety concerns' raised by US FDA and European medical agency. However long term follow up of patients with implanted Absorb stents will be continued. We have evaluated long term outcomes in Indian patients after implantation of bioresorbable stents as there is no such study till date.

Methods: This was a prospective, open label, single-center, observational clinical study. A total of 30 patients who had undergone PCI with bioresorbable stent (ABSORB) were reassessed at 3 years of follow up. These patients were evaluated for their functional status, stent thrombosis, in-stent restenosis (ISR), target vessel revascularization (TVR), myocardial infarction and death. Primary clinical endpoint was a composite of cardiac death, myocardial infarction or ischemia-driven target vessel revascularization at 3 years of follow up.

Results: The study population comprised of 87% males, 43% diabetics, 73% hypertensives and 20% smokers. Mean age was 60 years. Over 3 years of follow up, one patient (3.3%) expired due to noncardiovascular cause. Clinical ISR was seen in 2 patients (6.7%) and angiographic ISR in 4 patients (13.3%). Revascularization rate was 3.3% with target vessel revascularization of 3.3% and non target vessel revascularization of 0%. All target vessel revascularizations were due to restenosis related TLR. Primary composite endpoint of target vessel failure was seen in 3.3%. There was no incidence of stent thrombosis, non fatal MI and cardiac death during 3 years of follow up.

Conclusions: Long term clinical outcomes of our study are acceptable. There was no incidence of cardiovascular death, nonfatal MI or stent thrombosis during 3 years of follow up. Clinical restenosis was seen in 6.7% and angiographic restenosis in 13.3% of patients. Target lesion revascularization rate was 3.3%. Primary composite endpoint of target vessel failure was seen in 3.3% of patients.

Keywords: Bioabsorbable stents; Coronary artery disease; Stent thrombosis; In stent restenosis.

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Introduction

Coronary artery disease (CAD) is one of the important causes of demise in the world. Percutaneous coronary intervention (PCI) is one of

the mechanical interventions used for the treatment of CAD[1]. Bioabsorbable drug-eluting vascular scaffolds are a novel approach providing transient vessel support with capability of drug delivery. They are not associated with long-term limitations of metallic drug-eluting stents.[2] Permanent metallic stenting may preclude surgical revascularization, prevent late lumen enlargement, result in jailing of side branches, and interfere with noninvasive imaging of coronary arteries with multislice CT and MRI.[3,4]

Potential advantages of stent resorption at the treated site include decreased late stent thrombosis, improved lesion imaging with CT or MRI, facilitation of repeat revascularization (surgical or percutaneous) to the same site, restoration of vasomotor function, and freedom from side-branch occlusion by struts and from strut fracture-related restenosis.[5,6] Bioresorbable vascular scaffolds achieve successful acute revascularization of coronary lesions. Multiple imaging analyses have shown beneficial plaque stabilization and adequate sealing of intimal flaps caused by BVS-induced remodeling.[7] Serial intravascular imaging studies (IVUS / OCT) have demonstrated late lumen enlargement in numerous patients implanted with bioabsorbable stents.[6,8]

The Absorb BVS everolimus-eluting stent (Abbott Vascular) is the first bioabsorbable stent to demonstrate clinical and vascular outcomes similar to those following metallic drug-eluting stents for 2 years but with the potential advantages of full-stent absorption.[6,9] It is made of poly-D, L-lactic acid, its strut thickness is 150 µm, and it elutes a 1:1 mixtureof PLLA and the anti proliferative drug, everolimus. Complete hydrolytic degradation occurs over 3 years. In view of significantly different vascular response of bioabsorbable stents, it is quite mandatory to evaluate this in Indian patients too. Till date there is no such study in India, therefore very purpose of our study is to evaluate long term outcomes and safety profile of bioabsorbable stents in Indian patients.

Patients and methods

This was a prospective, open label, single-center, observational clinical study. The study was conducted in Advanced Cardiac Center of Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh from January 2016 to May 2017. Thirty patients were enrolled according to the following inclusion and exclusion criteria.

In brief, the inclusion criteria were patients at 18 years of age or older, with a diagnosis of stable, unstable, or silent ischemia that presented with a de novo lesion in a native coronary artery between 70% and 99% stenosis of the luminal diameter and a Thrombolysis In Myocardial Infarction flow grade of 1 or more, have undergone PCI with bioabsorbable stents and completed 3 years of follow up.

Exclusion criteria were patients with stenosis of the left main coronary artery, presence of intracoronary thrombus, heavy calcification, chronic total occlusions, in stent restenosis and bypass graft lesions. Study was approved by ethics committee. Written informed consent was obtained from each patient who participated in the study.

Patients who had undergone PCI with bioabsorbable stent (ABSORB) were evaluated at 3 years of follow up by means of clinical, noninvasive ± invasive cardiac testing. For each patient baseline characteristics like demographic data, coronary risk factors, comorbidities, routine blood investigations, baseline ECG, echocardiography, stress testing, coronary angiography findings and revascularization details were noted by reviewing patient records.At three years of follow up, these patients were reassessed withhistory, physical examination, ECG, 2D echocardiography and stress testing (TMT/stress thallium). Coronary angiogram was obtained in symptomatic patients and in patients with a positive stress test.

Endpoints and definitions

Patients were evaluated for their functional status, stent thrombosis, in-stent restenosis (ISR), target vessel revascularization (TVR), myocardial infarction and death.Timing of stent thrombosis was defined as acute (<24 hours), subacute (24 hours to 30 days), late (30 days to 1 year)and very late (beyond 1 year). Traditional definitions of stent thrombosis include only those episodes associated with an acute coronary syndrome and angiographic or pathologic demonstration of thrombosis within the stent or its margins. Clinical ISR was defined as the presentation of recurrent angina or objective evidence of myocardial is chaemia, whereas angiographic ISR was defined as the presence of >50% diameter stenosis in the stented segment. Target vessel revascularization (TVR) was defined as repeat revascularization (either repeat PCI or CABG) of the treated vessel. Primary clinical endpoint of the study was a composite of cardiacdeath, myocardial infarction or ischemia-

driven target vessel revascularization at 3 years of follow up.

Statistical analysis

Descriptive statistics were calculated for the various variables. They were presented as percentages and mean ± SD for qualitative and quantitative variables respectively. P value <0.05 was considered as statistically significant. All statistical analysis was done using SPSS version 24.

Results

Demographic profile

Age of the patients ranged from 46 to 85 years with mean of 60 years. Out of 30 patients 26 were males (86.7%) and 4 were females (13.3%). The coronary risk factors included diabetes mellitus (DM) in 13 (43.3%), hypertension (HTN) in 22 (73.3%), smoking in 6 (20 %), obesity in 4 (13.3%), dyslipidemia in 6 (20%) and family h/o coronary artery disease (CAD) in 3 patients (10%). There were all types of acute coronary syndrome presentations. 13 patients (43.3%) had ST elevation myocardial infarction. Of them 7 patients (23.3%) presented with acute anterior wall myocardial infarction and 6 patients (20%) presented with acute inferior wall myocardial infarction. Five patients (16.6%) had presented with unstable angina and 3 patients (10%) had Non ST elevation myocardial infarction. Remaining 9 patients had history of chronic stable angina with NYHA class II/III and were taken for coronary angiography after noninvasive evaluation.

Angiographic and procedural characteristics

Coronary angiography and PCI were performed as per current standards. Coronary angiogram revealed single vessel disease in 16 patients (53.3%), double vessel disease in 10 patients (33.3%) and triple vessel disease in 4 patients (13.3%). 26 patients (86.7%) had right dominant coronary circulation, 2 patients (6.7%) had left dominant and remaining 2 patients (6.7%) had co-dominant circulation. LAD was diseased in 25 patients (83.3%), LCX in 8 patients (26.7%) and RCA in 15 patients (50%). No patient had left main disease.

A total of 39 lesions were treated with ABSORB stents in 30 patients. Of these 39 lesions, 8 were type A (20.5%), 27 were type B (69.2%) and 4 were type C (10.3%) as per AHA (American Heart Association) classification of coronary lesions. PCI to Left anterior descending artery (LAD) was done in 23 (76.6%), left circumflex artery (LCX) in 4 (13.3%) and right coronary artery (RCA) in 8 patients (26.6%). All patients received ABSORB stents. Individual Stents were 18 mm and 28 mm long with diameters ranging from 2.5 to 3.5 mm (i.e. 2.5 mm, 3 mm and 3.5 mm). During the procedure, predilation and postdilation were performed in all patients. Maximum dilation pressure varied from 12 to 20 atm. Routine intracoronary imaging guidance was not used.

After stent deployment all patients had TIMI 3 flow. Angiographicsuccess was 100%. Dual antiplatelet therapy was continued for at least 1 year after the procedure. Procedural success and Clinical success were 100% each. Two patients (6.6%) developed minor bleeds in the form of small forearm hematoma in one patient and local oozing from femoral puncture site in the second patient which were managed conservatively.

Follow up

Clinical follow-up of the patients was conducted through regular follow up visits in the outpatient department. These patients were followed over a period of 3 years with range of 34 to 46 months and a mean of 39.3 ± 3.9 months.

At one year of follow up, coronary angiography and intracoronary imaging with OCT was done in 18 patients. On detailed evaluation of stent status, in stent restenosis was found in 2 patients. Target lesion revascularization was done in one patient in view of restenosis causing recurrent angina. One patient had expired due to lung cancer at 2 months of follow up (non cardiovascular death). There was no incidence of stent thrombosis, non fatal MI and cardiac death during 12 months of follow up. Apart from 3 major complications and 2 minor complications, reportedly there were no complications in the remaining 25 patients. Outcomes at one year of follow up are summarized in Table 1.

At 3 years of follow up, all patients (29) were reassessed with history, physical examination, ECG, 2D echocardiography and stress testing (TMT/stress thallium). Coronary angiogram was obtained in symptomatic patients and in patients with positive treadmill test (TMT)/stress thallium. Over 3 years of follow up, one patient (3.3%) had

expired due to non cardiovascular cause. There was no incidence of stent thrombosis, non fatal MI and cardiac death. Clinical ISR was seen in 2 patients (6.7%) and angiographic ISR in 4 patients (13.3%). Revascularization rate was 3.3% with target vessel revascularization of 3.3% and non target vessel revascularization of 0%. All target vessel revascularizations were due to restenosis related TLR. Primary composite endpoint of target vessel failure was seen in 3.3% Outcomes at three years of follow up are summarized in Table 2.

Table 1: Outcomes at one year of follow up.

Events at 365 days	Patients (%) (n= 30)
Death from any cause	1 (3.3%)
Cardiac death	0
Cardiovascular death	0
Noncardiovascular death	1 (3.3%)
Any nonfatal MI	0
Nonfatal target vessel MI	0
Nonfatal nontarget vessel MI	0
Any revascularization	1 (3.3%)
Target vessel revascularization	1 (3.3%)
Target lesion revascularization	1 (3.3%)
Stent thrombosis related TLR	0
Stent restenosis related TLR	1 (3.3%)
Nontarget lesion revascularization	0
Nontarget vessel revascularization	0
Any stent thrombosis	0
Definite stent thrombosis	0
Probable stent thrombosis	0
Possible stent thrombosis	0
Acute stent thrombosis	0
Subacute stent thrombosis	0
Late stent thrombosis	0
Very late stent thrombosis	0
In stent restenosis	
Clinical restenosis	1 (3.3%)
Angiographic restenosis	2 (6.7%)
Target vessel failure (composite endpoint)	1 (3.3%)

Table 2: Outcomes at 3 years of follow up.

Outcome	Patients (%) (n= 30)
Death from any cause	1 (3.3%)
Cardiac death	0
Cardiovascular death	0
Noncardiovascular death	1 (3.3%)
Any nonfatal MI	0
Nonfatal target vessel MI	0
Nonfatal nontarget vessel MI	0
Any revascularization	1 (3.3%)
Target vessel revascularization	1 (3.3%)
Target lesion revascularization	1 (3.3%)
Stent thrombosis related TLR	0
Stent restenosis related TLR	1 (3.3%)
Nontarget lesion revascularization	0
Nontarget vessel revascularization	0
Any stent thrombosis	0
Definite stent thrombosis	0
Probable stent thrombosis	0
Possible stent thrombosis	0
Acute stent thrombosis	0
Subacute stent thrombosis	0
Late stent thrombosis	0
Very late stent thrombosis	0
In stent restenosis	
Clinical restenosis	2(6.7%)
Angiographic restenosis	4 (13.3%)
Target vessel failure (composite endpoint)	1 (3.3%)

Discussion

This was a prospective, single group, open label, single centre, observational and clinical study of 30 patients conducted at Advanced Cardiac Center, PGIMER, Chandigarh to evaluate long term outcomes in Indian patients after PCI with everolimus eluting bioresorbable vascular scaffold (BVS).

At one year of follow up, coronary angiography and intracoronary imaging with OCT was done in 18 patients. On detailed evaluation of stent status, in stent restenosis was found in 2 patients. Target lesion revascularization was done in one patient in view of restenosis causing recurrent angina. One patient had expired due to lung cancer at 2 months of follow up (non cardiovascular death). There was no incidence of stent thrombosis, non fatal MI and cardiac death during 12 months of follow up.

Over 3 years of follow up, one patient (3.3%) expired due to noncardiovascular cause.Clinical ISR was seen in 2 patients (6.7%) and angiographic ISR in 4 patients (13.3%). Revascularization rate was 3.3% with target vessel revascularization of 3.3% and non target vessel revascularization of 0%.

All target vessel revascularizations were due to restenosis related TLR. Primary composite endpoint of target vessel failure was seen in 3.3%. There was no incidence of stent thrombosis, non fatal MI and cardiac death during 3 years of follow up.

So far the *Absorb Bioresorbable Vascular Scaffold (Abbott Vascular)* is the most evaluated bioabsorbable coronary stent. The ABSORB Cohort A[6,9] was the first-in-man trial to investigate the safety and feasibility of this everolimus-eluting BVS. At 2 years of follow up in ABSORB cohort A trial[8], the device was safe. There were no cardiac deaths, ischaemia-driven target lesion revascularizations, or stent thromboses. Only one patient had non-Q wave myocardial infarction (MACE rate was 3.3%). Even at 5 years of clinical follow up, the MACE rate was 3.3%. In our study, long term clinical follow up was conducted at 3 years after stent implantation. Major adverse cardiac event rate was 3.3%. However, angiographic ISR was seen in 13.3 % of patients.

ABSORB II trial[10,11] was the first randomized controlled comparison of a bioresorbable scaffold with a metallic stent. The primary endpoint was superiority of the Absorb for angiographic vasomotor reactivity. The co-primary endpoint was non-inferiority of angiographic late luminal loss. Acute lumen gain was lower for the bioresorbable scaffold by QCA as well as IVUS.

At one year of follow up[10], there were 17(5%) major cardiac adverse events in the absorb group and five events (3%) in thexience group (p=0•35). Scaffold thrombosis rate was 0.9% in the absorb group. In contrast there was no stent thrombosis in the xience group. In contrast to ABSORB II trial, one year outcomes of our study reported lower MACE rate of 3.3% with no incidence of stent thrombosis.

At 3 years of follow up[11], vasomotor reactivity was not statistically different. However target lesion failure occurred in 10% in the Absorb group and 5% in the Xience group. This was mainly driven by target vessel myocardial infarction (6% vs 1%). Over 3 years of follow up, Absorb group had eight cases of definite scaffold thromboses one case of probable scaffold thrombosis (3%). In contrast there was no device thrombosis in the Xience group (p value =0.0331).[11] These nine patients with scaffold thromboses suffered ST elevation myocardial infarction. One patient expired 13 days after scaffold thrombosis. Significantly increased device thrombosis rate particularly of late thrombosis was very alarming finding noticed in ABSORB II trial. In contrast to these alarming results, there were no episodes of devicethrombosis over 3 years of follow up in our study and MACE rate was 3.3%.

ABSORB III trial[12] was a large, multicenter, randomized trial involving 2008 patients with stable or unstable angina who were randomized in 2:1 ratio to receive Absorb scaffold or cobalt chromium xience stent. The primary endpoint of target vessel failure at 1 year was evaluated for both noninferiority and superiority. The primary composite endpoint occurred in 7.8% of patients in the Absorb group and 6.1% of the patients in the Xiencegroup (p value =0.007 for noninferiority, 0.16 for superiority). Device thrombosis within 1 year occurred in 1.5 % of patients in the Absorb group and in 0.7% of patients in the Xience group.[12] Authors concluded that treatment of noncomplex CAD with bioresorbable vascular scaffold as compared to metallic stent was noninferior with respect to target lesion failure at 1 year. In contrast, one year results of our study showed MACE rate of 3.3% with no incidence of stent thrombosis.

The recently available three-year follow-up data from the ABSORB III trial[13] continue to show an increased rate of major adverse cardiac events in BVS patients, when compared to patients implanted with the Xiencestent. Specifically, there was a 13.4% rate of major adverse cardiac events (e.g., cardiac death,myocardial infarction or ischemia-driven target vessel revascularization) in patients treated with the BVS at three years, compared with 10.4 percent in patients treated with Xiencestent (p = 0.056). The risk of BVS-treated patients developing scaffold thrombosis was higher than for patients treated with the Xiencestent. (2.3 % with BVS scaffold versus 0.7 % withXience stent at 3 years,p = 0.01).[13] Most cases of scaffold thrombosis occurred within the first year after BVS implantation, but beyond 1 year, the rate of new thrombosis events remained higher in BVS patients versus Xiencepatients. These results are in contrast to our study which reported MACE rate of 3.3% with no incidence of stent thrombosis at 3 years of follow up.

Limitations

Although there have been increased rates of scaffold thrombosis, particularly very late scaffold thrombosis with bioabsorbable stents as recently reported by ABSORB II trial (3 year outcomes),[11] ABSORB III trial (3 year outcomes),[13] ABSORB Japan trial (2 year outcomes)[14] and AIDA trial,[15] such complications were not seen in our study. However our study has got limitations, the most important limitation being its small sample size. Routine intravascular imaging in all the patients would have provided additional information.

Lastly being a nonrandomized study, it is subject to inherent limitations of all such studies.

Conclusion

Long term clinical outcomes of our study are acceptable. There was no incidence of cardiovascular death, nonfatal MI or stent thrombosis during 3 years of follow up. Clinical restenosis was seen in 6.7% and angiographic restenosis in 13.3% of patients. Primary composite endpoint of target vessel failure was seen in 3.3% of patients.

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Disclosure of conflicts of interest: None.

Ethical approval: PGIMER Chandigarh Ethics committee assessed and approved the study.

Informed consent: Informed consent was obtained from all the participants included in the study.

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