

Everolimus-eluting bioresorbable coronary scaffold in Asian patients: A 2-year follow-up

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Abstract

Indo-Pakistan population has one of the highest risk of coronary artery disease (CAD) in the world. Percutaneous interventions with the use of stents has been the mainstay of treatment for CAD, evolving from balloon angioplasty to bare metal stents and then to drug eluting stents. However, there are a few drawbacks related to the metal implant in the coronary, leading to the development of bio-resorbable vascular scaffolds (BVS). This case series studies the implantation techniques and 24 month clinical outcome of bioresorbable stent Absorb at Rawalpindi Institute of Cardiology. From November 1, 2013 till June 30, 2018. Fifty patients undergoing angioplasty with Absorb BVS as elective or primary PCI were enrolled. Case selection was at the discretion of the operator. Patients were followed up clinically. Repeat angiogram was conducted if clinically indicated. The study population involved patients with mean age of 42 ± 8.82 . Forty three (86%) were male and most had single or double vessel disease. The most common treated coronary was left anterior descending. Most of the lesions were predilated with 1:1 sizing. Most scaffolds were post dilated with 0.5mm larger diameter non-compliant balloon at nominal pressure. Angiographic success rate was 92%. On follow up, 4% had stent thrombosis (ST) (compared to <1% for latest generation drug eluting stents (DES) as per available literature). No death was reported. Majority of those with ST had longer median treated lesion length than those without stent thrombosis (32mm versus 28mm). Stent thrombosis occurred in 7.7% of cases with overlapping BVS while 2.8% in single BVS patients. To conclude, current generation Biovascular scaffold has higher thrombosis rates as compared to latest generation DES. Procedure/lesion related risk factors may predispose in addition to the thick stent struts.

Keywords: Bio-resorbable vascular scaffold, stent thrombosis, Absorb.

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Introduction

Coronary artery disease (CAD) is the leading cause of death worldwide being responsible for one in five deaths in US.^{1,2} Indo-Pakistani populations have very high risk of CAD in the world, one in five urban Pakistanis may have underlying CAD¹. WHO statistics of 2017 showed that 21.76% of total deaths in Pakistan are due to CAD.¹

Drug eluting stents (DES) have revolutionized the treatment of CAD. However, concerns of stent thrombosis (ST) remain mostly because of durable polymer inducing hypersensitivity reaction and poor healing.² In addition, DES leave metal residues in coronary arteries impairing vasomotion, remodeling and endothelial function.^{2,3} Bioresorbable vascular scaffold (BVS) is interesting alternative because the polymer prosthesis remains in the vessel only transiently. This allows for vessel function to return in addition to reducing inflammation.³ BVS provide support initially to prevent acute closure and release anti-proliferative drug to reduce neointimal hyperplasia, however get completely resolved in long-term. They allow surgical grafts to the stented segment of coronary as well as facilitate access to the jailed side branch after resorption.² Finally BVS have the advantage of reduced artifacts with noninvasive angiograms. Once the struts are resorbed they are replaced by neointima like the fibrous cap of atherosclerotic plaque.⁴ BVS may therefore offer advantage of stabilization of vulnerable plaque.⁴ Nevertheless concerns have been raised about increased stent thrombosis and other major adverse cardiac events (MACE) rate³. In addition higher profile of absorb BVS poses difficult deliverability.³

Absorb is a poly L-lactic acid polymer bioresorbable vascular scaffold. It is a balloon expandable scaffold with strut thickness of 150µm eluting everolimus with resorption time of 9 to 36 months depending on exact structure. Proper target lesion selection and preparation is mandatory for BVS implantation. The predilation balloon should be sized 1:1 and less than 40% residual stenosis aimed for after predilation.⁴ BVS expansion limit of 0.5 mm should not be crossed. Routine post dilation should be done. Absorb is the only FDA approved BVS, however in late 2017 it was withdrawn from market by

Abbott Vascular. Also results of Absorb III trial were discouraging. During the time it remained in market, thousands of patients all over the world had Absorb implanted, including Pakistan.

Case Series

Both elective and primary percutaneous coronary procedures, involving Absorb BVS implantation at Rawalpindi Institute of Cardiology over a 5 year period (November 2013-to June 2018) were studied. Procedure details were assessed. Patients were followed up clinically for 24 months for patient related outcomes including angina or hospital admission. Re-study of coronaries was performed with intravascular imaging, indicated by ischaemic symptoms. All patients were given dual antiplatelet for the standard duration of one year followed by lifelong aspirin alone. Outcomes were segregated as follows. The device success was defined as successful delivery and deployment of the scaffold at the intended target lesion. Angiographic success meant achievement of residual stenosis of less than 30% by visual estimation (or by quantitative method where needed), without significant dissection or no flow. Stent thrombosis was defined as documented scaffold thrombosis. Target lesion failure was defined as a composite of death, target vessel myocardial infarction or ischaemia driven target vessel revascularization at any time from absorb insertion till end of follow up at 24 months.

All the data was analyzed in the SPSS version 19. The data was checked for normal distribution by Shapiro Wilk test. A total of 50 cases entered the study. Table-1 shows the baseline characteristics of patients while Table-2 shows the details of implantation of scaffold and treated lesion. All cases had pre and post dilation done and intravascular imaging was not done. Amongst cases with overlapping

Table-2: Baseline characteristics of patients implanted Absorb BVS.

Variable	Value (mean±SD/percentage) OR Median (IQR)
Artery size(mm)	3.03±0.391
Lesion length (mm)	30.04± 14.31 / 28(18)
Treated lesion characteristics	
Calcification	1(2%)
Thrombus	10(20%)
Subtotal occlusion	3(6%)
Coronary stented	
LAD*	37(74%)
RCA**	8(16%)
LCX***	3(6%)
OM****/Diagonal	2(4%)
Overlapped BVS	13(26%)
Predilationballoonsizes BVS size	
Less than 1:1	23(46%)
1:01	27(54%)
Postdilationballoon vs stent size	
0.5mm larger	16(32%)
0.25mm larger	21(42%)
Equal size	13(26%)

*Left anterior descending, **right coronary artery, ***left circumflex, ****obtuse marginal.

BVS implantation, eleven cases(85%) had two scaffolds, while 2(15%) involved more than two overlapping BVS. In this overlapping cohort, 11(85%) involved overlapping BVS only, while two cases involved overlapping of BVS and DES. Device success was achieved in 49 cases(98%) while in one case the Absorb could not cross. Immediate result was optimal in 46 cases (92%) while one case(2%) had residual stenosis or dissection, one (2%) no reflow and one case(2%) strut fracture. Angiographic success was thus achieved in 92%. First two cases were managed well, however the case having strut fracture required bail out DES.

One case (2%) had early stent thrombosis within 30 days of the procedure. Over 24 months, two cases (4%) had target lesion failure due to myocardial infarction documented as stent thrombosis. There was no death. On follow up, 34 (68%) were asymptomatic, 6(12%) had nonspecific chest pain. Seven (14%) patients were lost to follow-up, while one had typical angina discomfort. Restudy was done in two patients (4%) due to symptoms that revealed patent scaffold. During restudy, intravascular imaging with OCT was done in one case (2%) showed patent and well apposed scaffold. Figure-1 show the BVS struts seen on OCT.

Stent thrombosis occurred in one out of 13cases (7.7%) with overlapping and one out of 37cases (2.8%) in non-overlapping scaffold patients, the difference was however

Table-1: Baseline characteristics of patients implanted Absorb BVS.

Variable	Value (mean±SD/percentage) OR Median (IQR)
Age	42 ± 8.82 / 45(15)
Male Sex	43(86%)
Extent of CAD	
DVCAD*	14(28%)
SVCAD**	36(72%)
Setting for PCI	
Primary PCI***	9(18%)
Stable IHD****	34(68%)
ACS*****	7(14%)
Follow up	24 months

*Double vessel Coronary artery disease, **Single vessel coronary artery disease, ***percutaneous coronary intervention, ****ischemic heart disease, *****Acute coronary syndrome.

statistically non-significant (p value=0.435). The median length of scaffold was 32mm in those with ST while 28mm in those without, with a non-significant p value=0.203. Similarly the stent size, post-dilation balloon size and the number of overlapped stents were not significantly different among those with or without ST (p value 0.399, 0.168 and 0.779 respectively). In both cases of stent thrombosis the pre-dilation balloon to stent size ratio was less than 1:1. In contrast among those without ST, the pre-dilation was done at 1:1 size in 28 cases (58%), the difference was non-significant however at $p=0.225$.

Discussion

Following most of the international studies on BVS, this series had patients with single or double vessel CAD, without left main stenosis. Majority were stable ischaemic heart disease (IHD) patients with simple target lesions, some had acute coronary syndrome (ACS). There is some encouraging data for BVS use in ACS.⁵ A meta-analysis including four RCT's showed comparable results of BVS absorb and xience, everolimus eluting metallic stent, for one year outcomes.⁶ However, only stable IHD patients were included, overlap was not allowed and treated lesion length was limited with mean length of 13mm.³ More patients were on potent antiplatelets like Ticagrelor or Prasugrel.³ Whereas in our series, sufficient percentage had acute coronary syndrome including primary PCI, quite some had overlapping scaffold and follow up was longer. Longer overlapped segment and certain lesion features mean greater the risk of stent thrombosis.^{2,3}

ABSORB II was the first randomized trial for Absorb scaffold and at one year results were similar for BVS and DES. However, it was under powered for 1 year outcomes and found a higher target lesion failure (TLF) in BVS as compared to xience at two years.⁷ ABSORB III reported BVS to be non-inferior to xience for TLF at one year.⁸ Stent thrombosis rate was higher with Absorb than with xience (1.9% versus 0.8%), although the difference was non-significant.⁸ In contrast, in our case series, suboptimal lesion preparation, lack of intracoronary imaging guidance for vessel sizing and long and complex lesions could explain higher ST. In three year results from ABSORB III the stent thrombosis rate may be disappointingly higher due to reasons like scaffold dismantling or positive remodeling of the vessel.^{8,9} Thus unless the scaffold is oversized, long-term outcomes will not be optimal. ABSORB IV initial results demonstrated that the Absorb stent implanted with optimized technique resulted in non-inferior 30-day and 1-year rates of target lesion failure and angina compared with DES.¹⁰ Three and five years follow-up results are yet awaited.

It is worth mentioning that Absorb, the first generation BVS was compared in above RCT's and meta analysis to the best third generation DES available with lowest documented stent thrombosis rate (0.85% overall ST in Absorb III). We know next generation BVS are under development.

Limited data is available for BVS use in small vessels, longer lesions or as overlapping or in the setting of STEMI.¹¹ Hybrid approach using BVS and DES has been found in literature with the proposed advantages of cost reduction and shorter length of metal.³ For calcific lesions, it is recommended only if adequate lesion preparation is achieved.³ We had one mildly calcific lesion treated successfully while in other Absorb could not cross. Ours had one case of hybrid with Absorb and xience.

Our series was limited by small sample size, lack of routine follow up angiogram and few clinical risk factors of ST and no fluoroscopic time studied. Larger population studies and longer follow up are needed to further elucidate the outcomes.

Proper lesion selection, adhering to recommended pre and post dilation techniques may avoid the higher MACE, as it has been shown to affect both acute results as well as clinical outcomes.¹² There is a longer learning curve for optimal implantation technique of BVS2. Probably higher strut thickness may be accounting for increased MACE in addition.¹³

We need to wait until long-term follow-up results from Absorb IV or registries come up with their long-term outcomes.

Conclusion

Current generation of BVS has higher rates of scaffold thrombosis as compared to internationally established stent thrombosis rates of latest generation drug eluting stents. Lesion selection, lesion preparation, BVS Implantation technique, post dilation and long lesion length requiring overlapping BVS remain the major risk factors in addition to the thick stent struts.

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Conflict of Interest: None to declare.

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