Cardiology and Cardiovascular Medicine

Volume 1, Issue 1

Short Communication

Clinical Outcomes From The Bioresorbable Vascular Scaffold: Is There A Role for Them?

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Received: 26 November 2016; **Accepted:** 02 December 2016; **Published:** 05 December 2016

Abstract

The risk of stent thrombosis and restenosis with the second generation drug eluting stents remains. The bioresorbable vascular scaffold is a third generation stent and overcomes the problems associated with drug eluting metallic stents. The bioresorbable vascular scaffold completely absorbs within the coronary vessel over 3-5 years. Multiple trials in patients with non complex coronary disease have demonstrated similar outcomes with regards to cardiac death, myocardial infarction and target vessel revascularisation when comparing the bioresorbable vascular scaffold with the second generation everolimus eluting metallic stents. However, the occurrence of device related thrombosis appears to be higher with the scaffold.

Keywords: Drug eluting stents; Bioresorbable vascular scaffold; Stent thrombosis; Intracoronary imaging

1. Introduction

Second generation drug eluting stents have consistently demonstrated better clinical outcomes when compared to bare metal stents and first generation drug eluting stents. Despite improvements in stent design the risk of restenois,

acute and late stent thrombosis remains. This is likely due to persistent inflammation from the presence of the metallic stent, stent fracture and tissue growth within the stent. There is also loss of the natural coronary vessel curvature once a metallic stent is deployed. Bioresorbable vascular scaffolds were developed to overcome the issues associated with drug eluting stents. Vasomotion i.e the ability of the vessel to dilate is believed to be restored with the bioresorbable vascular scaffold [1,2]. There is also improved endothelial function and the coronary vessel remodels once the scaffold is absorbed. However, successful deployment of a vascular scaffold involves several key steps including the use of intracoronary imaging for sizing of the vessel and to ensure adequate scaffold deployment.

2. Discussion

The bioresorbable poly (D, L-lactide) coating is 7-µm-thick and the scaffold is 150-µm-thick. The BVS elutes everolimus and has thicker stent struts when compared to the everolimus eluting metallic stent (EES). Complete resorption of the bioresorbable vascular scaffold (BVS) occurs over 3-5 years so that no substrate is present to allow restenosis which is seen with drug eluting metallic stents.

Deployment of a BVS requires adequate preparation of the culprit vessel. Guidelines from the BVS manufacturer recommend the 'PSP' technique in order to reduce the risk of scaffold thrombosis. This consists of adequate pre dilatation of the culprit vessel, appropriate sizing of the vessel prior to scaffold deployment and finally post dilatation of the deployed BVS.

Pre-dilatation consists of using a 1:1 balloon to artery ratio using non compliant balloons. The use of intravascular ultrasound (IVUS) or optical coherence tomography (OCT) should be considered for sizing the vessel. Once deployed the scaffold should be post dilated with a non compliant balloon up to 0.5mm above the nominal scaffold diameter. Residual stenosis after deployment should be <10%, which can be measured on IVUS/OCT. BVS thrombosis has been reported in 1.8% of patients at 30 days and 3% at 12 months. Several mechanisms for BVS thrombosis have been identified including early discontinuation of dual antiplatelet therapy, lower post procedural minimal luminal area (p=<0.0001) especially if the vessel diameter was <2.4mm for the 2.5-3mm BVS or diameter <2.8mm for the 3.5mm BVS scaffold. When the 'PSP' protocol was followed rates of scaffold thrombosis reduced at 1 year from 3.3% to 1.0% (p=0.012) [3].

Several trials have compared outcomes of the BVS with the second generation everolimus eluting metallic stents. The ABSORB II trial was the first trial to compare the BVS with the EES. Randomization of 501 patients occurred in a 2:1 ratio to the BVS group and the EES group. There were 335 patients with non complex coronary disease in the BVS group and 166 patients in the EES group. The primary end point was to assess for coronary vasomotion i.e the change in mean lumen diameter, by administering intracoronary nitroglycerine. Vasomotion with the BVS was not superior to the EES. Post dilatation balloon pressure was highest in patients in the EES group. Acute recoil post deployment defined as the difference between the maximum balloon size minus the residual minimum diameter, was similar between both devices. Acute lumen gain for the BVS was lower than the EES when using quantitative

coronary angiography or IVUS; 1.15 mm versus 1.46 mm respectively when using quantitative coronary angiography (p=<0.0001). On IVUS acute lumen gain was 2.85 mm^2 versus 3.60 mm^2 respectively, (p=<0.0001). 22% of patients in the BVS group had anginal symptoms at one year follow up versus 30% in the EES group (p=0.04). However exercise performance was similar between both groups when tested. The cause for the reduction in anginal symptoms in the BVS group was unclear but it has been proposed that the flexibility of the BVS may account for the reduction in anginal symptoms i.e the ability of the BVS to take the natural curvature of the coronary artery when compared to the metallic stents. The degradation of the scaffold over time may allow the coronary to dilate and restore natural vasomotion whereas this is not possible with the metallic stent. At 1 year stent thrombosis occurred in three patients in the BVS group and no patients in the EES group. Major adverse cardiovascular events were encountered in 5% of patients who received the BVS and 3% of patients in the EES. Myocardial infarction rates were 4% versus 1% respectively and target lesion revascularisation was indicated in 1% and 2% of patients respectively. Therefore, the clinical endpoints at 1 year were similar for the BVS and the EES [4]. Recent published 3 year follow up data from the ABSORB II trial did not demonstrate any significant improvement in vasomotor tone and there was increased late lumen loss when compared to the EES. Target vessel myocardial infarction was significantly higher in the BVS group at 7% versus 1% (p=0.006). Late stent thrombosis was also higher in the BVS group when compared to the EES. Therefore, longer term outcomes were worse in the BVS group [5].

Further trials such as the ABSORB III trial assessed the safety and effectiveness of the BVS with the EES in patients with non complex coronary disease. As per the ABSORB II trial patients were randomized in a 2:1 fashion to receive the BVS or the EES. Patients with a diagnosis of non-ST segment elevation myocardial infarction and ST segment elevation myocardial infarction were excluded. For enrollment into the trial the coronary lesion had to be no longer than 24mm in length and had to be 2.5-3.75mm in diameter assessed using angiography. Pre-dilatation of the lesion was recommended when using the BVS. Post dilatation after deployment of the BVS and EES was preferred in order to achieve <10% residual stenosis for both devices. Expansion of the BVS no more than 0.5 mm above the nominal scaffold diameter was advised to prevent strut fracture. The primary end point of target lesion failure at 1 year occurred in 7.8% of patients in the BVS group and 6.1% in EES group (p=0.007 for non inferiority). There was no difference between both devices at 1 year for the rates of angina, total revascularization, and ischemia driven target vessel revascularization, which is consistent with the results from previous trials [4,6,7]. Stent thrombosis at 1 year occurred in 1.5% of patients in the BVS group and 0.7% of patients in the EES group (P=0.13). However, the rates of subacute stent thrombosis (>24 hours-30days) were significantly higher after implanting the BVS. This may be due to higher rates of residual stenosis within the device post procedure due to the greater strut thickness or recoil. Although the trial demonstrated non inferiority to EES it is important to note that both ABSORB II and III restricted enrollment to patients with non complex coronary disease with stable symptoms, therefore the results cannot be applied to all patients seen on a daily basis. Patients with an ST elevation myocardial infarction and non-ST elevation myocardial infarction were excluded and it is often these patients that require coronary revascularisation. Further exclusions were applied to patients with left main stem disease, the presence of moderate to heavy calcified coronary arteries, bifurcation lesions and chronic total occlusions. Finally the trial was

underpowered to assess for cardiac death and stent thrombosis [8]. The ABSORB IV trial is an ongoing trial and an extension of ABSORB III and will look at 5 year outcomes in patients treated with a BVS.

The ABSORB China trial was conducted to seek approval of the BVS in China. Patients with non complex coronary disease were randomized to receive the BVS or EES. The primary end point was angiographic in segment late loss . 480 patients were randomised with 241 patients to BVS and 239 to the EES. Late lumen loss for BVS was non inferior to the EES. Target lesion failure defined as the composite of cardiac death, target vessel myocardial infarction or ischaemia driven target lesion revascularization was similar between both groups, 3.4% for BVS and 4.2% for EES (p=0.62). Rates of stent thrombosis were 0.4% and 0% respectively (p=1.00) [9]. At 2 years follow up the clinical event rates were similar for both devices. All cause death, myocardial infarction and revascularisation was 10.1% for the BVS and 11.4% for the EES. Scaffold thrombosis was 0.8% versus 0% respectively (p=0.5) which was lower than that reported in ABSORB II [10].

In a meta-analysis of 3738 patients randomised to receive the BVS or the EES, the rates of target lesion revascularization, target lesion failure, myocardial infarction and death were similar between both groups at 1 year. However, there were higher rates of definite or probable stent thrombosis in patients treated with the BVS within the first 30 days of deployment [11].

In registries no significant differences in adverse events have been reported between the BVS and EES at 1 year. The main limitation of these trials was the low number of patients recruited and therefore not adequately powered for the detected clinical end points [4, 6,7]. In a further registry of patients treated with the BVS, outcomes including a composite of cardiac death, target vessel myocardial infarction, and ischaemia driven target lesion revascularization at 1 year follow up was 5.8% with the BVS versus 7.6% with the EES (p=0.12). Cardiac death was less likely in the BVS group; 0.7% versus 1.9% (p=0.03). There was no difference in the rates of device related thrombosis; 1.8% for BVS and 1.1% for EES [12].

Data regarding outcomes with the use of the BVS in patients with ST segment elevation myocardial infarction (STEMI) is scarce. In a retrospective observational study outcomes in patients with a STEMI who received either a BVS, EES or bare metal stent (BMS) were assessed. Patients were matched according to baseline characteristics and presentation. 290 patients in each arm were matched. Balloon pre-dilatation was not mandatory but was recommended in patients who had a BVS. Pre and post balloon dilatation was higher in the BVS compared to the EES and BMS. The combined primary end point of cardiac death, target vessel myocardial infarction and target vessel revascularisation at 1 year did not differ between the stent types at 30 days or 1 year. The primary end point occurred in 3.1%, 2.4% and 2.1% in the BVS, EES and BMS group respectively at 30 days. At 1 year the primary end point was 4.1%, 4.1%, and 5.9% respectively. Scaffold thrombosis was higher at 30 days and 1 year when compared to the DES or BMS although not statistically significant [13]. Due to the low number of patients recruited the results may not be applicable to everyday practice.

Several trials have demonstrated similar outcomes of the BVS when compared to the EES. However, it is important to note that low number of patients were recruited in these trials. Furthermore, patients had non complex coronary disease and patients with a myocardial infarction, left main stem disease and presence of moderate to heavy calcification were generally excluded. The BVS is limited in its size as it can only be used in lesions <24mm in length and with a diameter of >2.5-3.75mm. The deployment of a scaffold prolongs procedure time since adequate pre-dilatation of the culprit vessel is required as well as intracoronary imaging to ensure adequate scaffold deployment. The scaffold may be therefore be suited in younger patients with non complex coronary disease who may require coronary artery bypass graft surgery in the future where a metallic may hinder graft positioning on the vessel

3. Conclusion

Trials comparing the bioresorbable vascular scaffold with the everolimus eluting metallic stent have demonstrated similar short term outcomes when used in patients with non complex coronary disease. Early scaffold thrombosis is of concern, although the reasons for this are unclear. Larger recruitment and long term follow up is required to assess the safety of the bioresorbable vascular scaffold.

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