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TRANSLATIONAL

Vasomotor Function Comparative Assessment at 1 and 2 Years Following Implantation of the Absorb Everolimus-Eluting Bioresorbable Vascular Scaffold and the Xience V Everolimus-Eluting Metallic Stent in Porcine Coronary Arteries

Insights From In Vivo Angiography, Ex Vivo Assessment, and Gene Analysis at the Stented/Scaffolded Segments and the Proximal and Distal Edges

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ABSTRACT

OBJECTIVES The purpose of this study was to assess and compare in vivo the restoration of vasomotor function following Absorb bioresorbable vascular scaffold (BVS) (Abbott Vascular, Santa Clara, California) and metallic Xience V (XV) (Abbott Vascular, Santa Clara, California) stent implantations in porcine coronary arteries at 1 and 2 years.

BACKGROUND Drug-eluting metallic coronary stents induce sustained vasomotor dysfunction, and preliminary observations from arteries with bioresorbable scaffolds have indicated partially restored vasoreactivity.

METHODS A total of 15 Absorb BVS (3.0 × 18.0 mm) and 14 XV (3.0 × 18.0 mm or 3.0 × 12.0 mm) stents were randomly implanted in the main coronaries of 12 nonatherosclerotic swine. The effect of implant on vasomotor performance (constrictive and expansive) was measured in the stented/scaffolded segments and the 5-mm proximal and distal adjacent segments in vivo by angiography assessing mean luminal diameter changes following infusion of vasoactive agents at 1 year (n = 6) and 2 years (n = 6) as well as ex vivo at 2 years using a tissue chamber apparatus. Endothelial cell function and smooth muscle cell phenotype gene marker levels were evaluated with quantitative real-time polymerase chain reaction.

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RESULTS The scaffolded Absorb BVS segments showed fully restored constrictive response compared with XV implanted vessels at 1 year: −24.30 ± 14.31% versus −1.79 ± 6.57% ($p < 0.004$) and at 2 years: −28.13 ± 14.60% versus −3.90 ± 6.44% ($p < 0.004$). The early restoration of vasomotor function within the scaffolded segments reached a peak at 1 year and did not significantly change up to 2 years. The vasoactive responses of Absorb BVS-implanted vessels within the scaffolded segments were similar to those observed within the proximal and distal edge segments at both time points. Conversely, the stented XV segments demonstrated significantly impaired constrictive response compared with the distal XV edges at 1 year: −1.79 ± 6.57% versus −21.89 ± 7.17% ($p < 0.0002$) and at 2 years: −3.90 ± 6.44% versus −21.93 ± 15.60% ($p < 0.03$). Ex vivo assessment of contraction induced by PGF2α and relaxation induced by substance P of isolated BVS segments compared with XV-treated segments generated greater contraction force of 3.94 ± 0.97 g versus 1.83 ± 1.03 g ($p < 0.05$), and endothelial-dependent relaxation reached 35.91 ± 24.74% versus 1.20 ± 3.79% ($p < 0.01$). Quantitative real-time polymerase chain reaction gene analysis at 2 years demonstrated increased Connexin 43 messenger ribonucleic acid levels of Absorb BVS-treated vessels compared with XV-treated vessels: 1.92 ± 0.23 versus 0.77 ± 12 ($p < 0.05$).

CONCLUSIONS Absorb BVS-implanted coronary arteries demonstrate early functional restoration of the scaffolded and adjacent segments at 1 year, which is preserved up to 2 years. (J Am Coll Cardiol Intv 2016;9:728–41) © 2016 by the American College of Cardiology Foundation.

Despite innovations in the field of coronary stenting, clinical restenosis and stent thrombosis rates following stent deployment in diseased coronary arterial segments remain at 5.0% and 0.4%, respectively. Furthermore, late or very late clinical events attributed to in-stent neoatherosclerosis, very late stent thrombosis, and endothelial dysfunction are being increasingly observed (1-3).

Permanent metallic drug-eluting stents (DES) with durable polymer coatings induce sustained endothelial- or nonendothelial-dependent vasomotor dysfunction after revascularization both within and distal to the implanted segments, which invariably extends during the healing phase (4,5). Endothelial dysfunction attributed to direct diffusion of the antiproliferative agent distal to treated segments or indirectly through vasa vasora remains the prevailing pathogenic mechanism. Preliminary observations from newer-generation DES have demonstrated relatively preserved endothelial-dependent vasomotor function at the proximal and distal edges compared with earlier-generation devices, whereas the in-stent segments remain dysfunctional (6).

Bioresorbable scaffolds provide a platform for vascular reparation by enabling anatomic and functional restoration during the healing phase subsequent to gradual scaffold resorption (7). Preliminary evidence derived from prospective registries, such as the ABSORB Cohorts A and B, have indicated significant anatomic and functional recovery of vessels treated with a fully resorbable scaffold during the later phases of vessel reparation (8-10).

There is a paucity of experimental comparator observations assessing short- and long-term vascular responses following deployment of permanent metallic stents and fully resorbable scaffolds in the absence of underlying atherosclerosis (11-13). Accordingly, we investigated the vasomotor and genetic responses of porcine coronary arteries treated with a permanent metallic DES, the Xience V (XV) stent (Abbott Vascular, Santa Clara, California), and a fully resorbable scaffold, the Absorb bioresorbable vascular scaffold (BVS) (Abbott Vascular, Santa Clara, California), at 1 and 2 years.

We hypothesized that Absorb BVS-treated coronary segments will demonstrate more robust functional and phenotypic recovery compared with XV-treated vessels.

METHODS

ANIMALS AND EXPERIMENTAL PROTOCOL. The study protocol was approved by the Institutional Animal Care and Use Committee and was conducted in accordance with the Association for Assessment and Accreditation of Laboratory Animal Care guidelines. Twelve healthy juvenile Yucatan mini swine (Sinclair Bio-Resources, Columbia, Missouri) underwent implantation of 15 Absorb BVS (3.0 × 18 mm) and 14 XV stents (3.0 × 18 mm and 3.0 × 12 mm) in their main coronary arteries. The lack of atherosclerosis in our model was purposely designed to investigate the differences in vasomotor function between Absorb BVS- and XV-treated vessels avoiding the