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EDITORIAL COMMENT

Bioresorbable Vascular Scaffolds

A Step Closer to the Dream?*

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Some physicians can be inadvertently short sighted. But patients have to live with our treatment effects for a lifetime. For a typical 60- to 65-year-old percutaneous coronary intervention patient, the common 1-year "horizon" for drug-eluting stent (DES) outcomes, needs to be extended to more akin to that of our surgical colleagues—10 years and beyond.

The dream of bioresorbable stents (BRS) is to serve as a DES when needed and dissolve when it is not, thereby attenuating or eliminating the seemingly unending 2% to 2.5% per year incidence of stent-related target lesion failure (TLF) after year 1 (1,2), ascribed to late inflammation, neoatherosclerosis, strut fracture, or late drug effect.

Current bioresorbable vascular scaffolds (BVS) are largely covered by endothelium by 28 days, begin losing their scaffold supportive capacity by 12 months, and are fully resorbed in most humans by about 3 years (3,4). Return of cyclic pulsatility may be correlated with the observed change from the proliferative to the contractile smooth muscle cell phenotype observed in animal studies (4). Yet we have limited high-quality data in large numbers of patients for TLF beyond 2 to 3 years (5,6). Admittedly, cases of very late scaffold thrombosis have already been reported (5,6).

Contemporary BVS approach second-generation DES's first-year device outcomes when used in moderate diameter to large vessels and with good technique (7,8), but they are clearly more thick-strutted than ideal. More streamlined devices will surely follow.

Yet the essential question remains—if and when will the BVS/BRS event rate drop below that from the best DES? Can we glean an impression of the answer to this question on the basis of late imaging or physiologic studies in modest numbers of patients?

Serruys et al. (9) recently reported imaging results at 5 years from the Absorb cohort B study. Recalling that these patients and lesions were relatively uncomplicated and simple, 60-month late loss was 0.26 mm, with minimal changes after 12 months. This was confirmed by optical coherence tomography, which also demonstrated a thick-capped neointima in most patients. Vessels were also noted to be progressively more responsive to nitroglycerin. Adverse clinical events between 1 and 5 years were uncommon, with no scaffold thromboses and only 4% ischemia driven target lesion revascularization.

Dudek et al. (10) provide further details in this issue of *JACC: Cardiovascular Interventions*. Unpaired angiographic responses to intracoronary nitroglycerin were compared 2, 3, and 5 years after scaffold implantation. Maximum, but not mean, lumen diameter change increased significantly over time, although the overall response was only about one-half of that seen in adjacent untreated segments.

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Although perhaps this report could have been strengthened by providing details about possible nitrate tolerance, atherosclerosis at adjacent sites, having paired comparisons and including all patients, as well as testing with more prognostic endothelium-dependent stimulators, the results are of interest.

Epicardial coronary vasomotion is regulated by endothelial mediators (e.g., thrombin, angiotensin, acetylcholine), and the response of vascular smooth muscle to factors such as endothelin-1, nitric oxide, and PGI_2, as well as neurotransmitters (principally norepinephrine). Vascular responses to stimulants

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are often divided into those that are endothelium dependent (e.g., acetylcholine) and endothelium independent (nitroglycerin). Human coronary arteries exhibit a dose-response effect to the former. Healthy arteries dilate with low doses and constrict with higher doses. Visibly diseased arteries and those exposed to CAD risk factors constrict to acetylcholine even at low doses, and this response has been used to identify diseased arteries in the cath lab as well as predict long term CAD-related prognosis (11,12).

All cardiologists know that coronary arteries should vasodilate in response to nitroglycerin. Less well recognized is the predictive information gained from the degree of vasodilation. Several modest-size studies concordantly confirm that more is better in terms of reducing later risk of cardiovascular death and myocardial infarction, although the magnitude of correlation is less than that with acetylcholine response (12–15). For example, von Mering et al. (12) studied 163 women from the WISE (Women's Ischemia Syndrome Evaluation) study. Hazard ratios for adverse cardiovascular events at 3 years for patients with abnormal response to acetylcholine and nitroglycerin at years were 1.6 and 1.5, respectively, although only that to acetylcholine was statistically significant in the final multivariate model (12). Schachinger et al. (13) studied 147 patients and found 7.7-year cardiovascular outcomes to be correlated with both acetylcholine ($p = 0.009$) and nitroglycerin ($p = 0.001$) response.

Does the fact that post-BVS coronaries dilate more to nitroglycerin at 5 than 3 years, with both times well beyond when scaffolding function should be gone, mean that the arteries are getting healthier over time? Or is this simply a manifestation of the late effects of resolution of residual proteoglycan that had infiltrated the BVS site? That said, BVS-treated sites still only dilated to 42% to 57% as much as adjacent nontreated sites. Is the thick-capped as opposed to thin-capped neointima protective against plaque rupture-related events?

Whether or not these findings in medically treated patients with generally modest degrees of atherosclerosis (12–15) translate to events related to previously BVS-treated artery sites remain, of course, to be determined.

Do Dudek et al. (10) bring us a step closer to the dream? No, but perhaps a half or quarter step. At least it is in the right direction.

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