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REVIEW TOPIC OF THE WEEK

Current Status of Bioresorbable Scaffolds in the Treatment of Coronary Artery Disease

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ABSTRACT

State-of-the-art drug-eluting metal stents are the gold standard for interventional treatment of coronary artery disease. Although they overcome some disadvantages and limitations of plain balloon angioplasty and bare-metal stents, some limitations apply, most notably a chronic local inflammatory reaction due to permanent implantation of a foreign body, restriction of vascular vasomotion due to a metal cage, and the risk of late and very late stent thrombosis. The development of biodegradable scaffolds is a new approach that attempts to circumvent these drawbacks. These devices provide short-term scaffolding of the vessel and then dissolve, which should theoretically circumvent the side effects of metal drug-eluting stents. Various types of these bioresorbable scaffolds are currently under clinical evaluation. This review discusses different concepts of bioresorbable scaffolds with respect to material, design, and drug elution and presents the most recent evidence. (J Am Coll Cardiol 2014;64:2541–51) © 2014 by the American College of Cardiology Foundation.

New techniques for interventional treatment of coronary artery disease are continuously being developed. Important milestones include the launch of balloon angioplasty in 1977, the introduction of bare-metal stents in the 1980s, and the application of drug-eluting stents (DES) since 2000. DES were widely investigated in different settings, demonstrated clinical success, and entered into clinical guidelines as the treatment of choice for interventional revascularization of coronary artery stenosis (1,2). DES overcame disadvantages, such as acute vessel recoil and dissection risk after plain balloon angioplasty and decreased myocardial infarction and target lesion revascularization (TLR) rates compared with bare-metal stents due to reduced neointimal tissue growth (3). Despite these and other benefits, some concerns remain: the risk of late and very late stent thrombosis; continued neointimal tissue growth and neoatherosclerosis; malapposition; potential stent fracture; incomplete endothelialization; and vessel caging causing abnormal vasomotion.

An anticipated major cause of late and very late DES thrombosis is impaired arterial healing, possibly due to the durable coating, which results in a chronic inflammatory reaction with incomplete stent endothelialization and persistent fibrinogenesis and platelet aggregation, affecting blood flow and vessel remodeling (4–7). Next-generation metal stents with biodegradable polymer coatings are designed to overcome these shortcomings. A trial that randomly assigned patients to percutaneous coronary intervention (PCI) with DES with either a bioresorbable polymer coating or a durable coating demonstrated a significantly

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ABBREVIATIONS AND ACRONYMS

BRS = bioresorbable scaffold(s)

BVS = bioresorbable vascular scaffold

CE = Conformité Européenne

DES = drug-eluting stent(s)

IVUS = intravascular ultrasound

MACE = major adverse cardiac event(s)

OCT = optical coherence tomography

PCI = percutaneous coronary intervention

PLLA = poly-L-lactic acid

TLR = target lesion revascularization

lower rate of definite very late stent thrombosis with the bioresorbable polymer coating during a 4-year follow-up (8). Additionally, improved vasomotion and endothelialization was seen (9,10), although hard endpoints (e.g., myocardial infarction, TLR, cardiac death) did not differ significantly (8,11). In another randomized, controlled trial, no significant differences were observed in outcomes between DES types during a 3-year follow-up (12). Furthermore, a recent meta-analysis revealed nonsuperiority, even inferiority, of DES coated with bioresorbable polymer compared with cobalt-chromium everolimus-eluting stents (13). In addition to the need for more long-term data, further challenges must be addressed to improve preliminary results. Nevertheless, this stent type cannot resolve long-term vessel caging and the side effects associated with permanent implants.

The next interventional cardiology advance may be the introduction of bioresorbable scaffolds (BRS). The term *scaffold* highlights the temporary nature of a BRS, distinct from a stent associated with a permanent implant. All resorbable scaffolds are commonly referred to as *bioresorbable*, even though some are not made of biomaterials.

The idea of dissolvable scaffolds is not new, dating to the description of Tamai et al. (14) of the first successful use of a fully degradable stent in the early 1990s. However, this concept was nearly forgotten due to the success of bare-metal stents and, later, DES. With long-term data and the revelation of the risks of metal stents, BRS development was reinitiated, resulting in a variety of devices.

MATERIAL COMPOSITION AND PROPERTIES

The optimal BRS should ensure adequate short- to mid-term scaffolding of the previously stenosed vessel to avoid recoil and completely dissolve afterward to prevent side effects. Thus, temporarily sufficient radial support is needed, with struts as thin as possible. The design should warrant deliverability and straightforward handling, flexibility in different anatomic circumstances, and integrity during resorption. The optimal duration until full resorption is not yet defined. To achieve these goals, a considerable variety of materials and designs are under investigation.

Furthermore, the use of drug elution is inconsistent. Several different substances have been applied, and some BRS are noneluting. The current trend is toward broader use of drug elution, with mTOR (mammalian target of rapamycin) inhibitors as the most frequently used antiproliferative drugs in DES.

The **Central Illustration** provides an overview of different designs and characteristics of existing BRS, with representative images in **Figures 1 and 2**.

POLY-L-LACTIC ACID. Different materials are used for manufacturing BRS, with poly-L-lactic acid (PLLA) being the most commonly used. For most existing PLLA-based devices, strut thickness is 150 μm. A BRS currently being developed has the thinnest struts (100 μm) of all BRS, irrespective of composition. According to the manufacturer, a PLLA-based scaffold has radial strength comparable to that of current drug-eluting metal stents. Directly after implantation, radial strength is ~1,200 mm Hg, and the observed radial force can still be as great as 800 mm Hg after 1 year. Degradation by hydrolysis of interlactic bonds of the long PLLA chains results in particles that macrophages can phagocytose. The end product is lactic acid, metabolized via pyruvate into carbon dioxide and water through the Krebs cycle (15), with complete degradation achieved in 1 to 3 years (**Central Illustration**). **Figure 3** shows degradation over time of the BRS compared with the Xience DES (Abbott Vascular, Santa Clara, California). PLLA-based devices ensure radial support for ~6 months.

MAGNESIUM. Magnesium, complemented by rare earth metals to improve radial strength, is another currently used BRS production base. The first magnesium-based scaffolds were uncoated and lacked antiproliferative drug elution. The underlying idea is that the electronegative charge that emerges during the degradation of metal BRS is antithrombotic (16,17). A further potential benefit is its high mechanical strength, making it a stent with thinner struts, but radial strength similar to that of other bioresorbable scaffolds, possible. Depending on composition, degradation takes between 2 and 12 months. The products of stent dissolution by corrosion are inorganic salts (17). The latest generation device offers 9 to 12 months of radial support (18).

OTHER MATERIALS

A tyrosine polycarbonate-based BRS providing up to 6 months of radial support is also under investigation. Resorption takes between 24 and 36 months. Final products of degradation, which starts with hydrolysis and ends with the Krebs cycle, are ethanol, water, and carbon dioxide (19).

A BRS made of polylactic anhydride containing 2 salicylic acid molecules linked to 1 sebacic acid