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Latest-Generation Drug Eluting and Bioabsorbable Stents

Eleftherios Tsiamis, MD

First Department of Cardiology, Ippokratio University Hospital, Athens, Greece

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ABBREVIATIONS
DAPT = dual antiplatelet therapy
DES = drug-eluting stent(s)
mTOR = mammalian target of rapamycin
PCI = percutaneous coronary intervention
PTCA = percutaneous transluminal coronary angioplasty

Correspondence to:
Eleftherios Tsiamis, MD
E-mail: ltsiamis@otenet.gr

Percutaneous transluminal coronary angioplasty (PTCA) was introduced in the late 1970s as an alternative to coronary artery bypass graft surgery for coronary revascularization; since then, it has been accepted as a safe, reliable, and effective treatment for coronary artery disease, and its use has spread worldwide. The introduction of first-generation drug-eluting stents (DES) transformed the practice of percutaneous coronary intervention (PCI) by drastically reducing the rate of in-stent restenosis. The efficacy of DES has largely been demonstrated in large randomized trials, leading to their current widespread use in clinical practice.

First- and second-generation DES have three major components, the stent platform, the antiproliferative drug, and the polymer. The stent platform is the scaffold of the stent. It provides the radial force to prevent vessel occlusion provoked by vessel injury following PCI. First-generation DES used stainless steel platforms. Cobalt-chromium and later platinum-chromium platforms used in second-generation DES permitted similar stents' radial strength, while enabling a thinner strut design and subsequently significantly improved deliverability. Recently, bioabsorbable platforms that biodegrade over a period of months have been developed, with the purpose of allowing the restoration of a normal vascular physiology and function over time. Ultimately, no foreign material is left exposed in the bloodstream. These stents may also potentially preserve reactive vasomotion and permit expansive remodeling.

There are several antiproliferative drugs with different modes of action. The goal of these drugs is to inhibit vascular smooth cell proliferation and migration, without affecting endothelial regeneration, and have anti-inflammatory/anti-thrombotic properties. Inhibitors of the mammalian target of rapamycin (mTOR) are the dominant class of antiproliferative drugs used for DES. The first mTOR inhibitor used in clinical practice was sirolimus. First generation DES also used paclitaxel, which is a taxan drug, which acts as a cytotoxic drug through the stabilization of microtubules. Later derivatives include zotarolimus and everolimus (mTOR) and tacrolimus, which acts as a calcineurin inhibitor, and is a cytostatic agent with both antiproliferative and anti-inflammatory activities However, all these antiproliferative agents have shown detrimental local effects on the vascular wall and on endothelial function recovery after stenting. New drugs (biolimus, novolimus, and myolimus) have been developed and have shown promising results.

Stent polymers control elution of the antiproliferative drug over a variable period of time. Once drug elution has been completed, most polymers exert limited functions and act as a potential trigger for local inflammation and hypersensitivity. The biocompatibility, composition, formulation, degradation delay of the polymer, pharmacokinetics of the antiproliferative agent released by the polymer, and the management of variation in polymer degradation delay have become new difficult challenges

for the development of stent polymers. An optimal polymer should mimic the endothelial lining in order to prevent late thrombotic complications, thus improving stent safety. Third-generation DES use polylactic acids (poly-L-lactic acid and poly D,L-lactide-co-glycolide) as bioabsorbable polymers. Finally, another field of research is the development of stents that elute antiproliferative drugs without the need for polymers. Preclinical studies support their use, but robust data are still lacking.

Current guidelines support the use of dual antiplatelet therapy (DAPT) for 6–12 months after DES implantation. In 2006, the potential risk of late/very late stent thrombosis after DES implantation raised the question of prolonging DAPT even beyond the first year. However, prolonged DAPT has also clearly been associated with an increased risk of bleeding. Availability of new biodegradable polymers and/or stents may shorten the duration of necessary DAPT and therefore minimize the risk of major bleeding to which it is associated.