Complex Coronary Intervention in the Drug-Eluting Stent Era

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"If I had an enemy, I would teach him angioplasty."
Andreas Gruentzig, MD, 1980

With these words, Andreas Gruentzig depicted the emotional anguish and uncertainty produced by the inflation of a fluid-filled balloon in the human coronary artery. Indeed, in the era prior to coronary stenting and optimal adjunctive pharmacotherapies, abrupt coronary occlusion complicated 4% to 8% of balloon angioplasty procedures, was unpredictable in occurrence, and was associated with significant morbidity and mortality for the patient. The advent of coronary stents, which provide a scaffold for balloon-mediated plaque disruption, prevent immediate arterial recoil, and promote laminar coronary flow, has reduced the risk of procedural complications. Furthermore, multiple randomized, controlled trials comparing coronary stent deployment to balloon angioplasty have demonstrated the salutary effect of stents in reducing late (≥ 6 months) coronary restenosis/occlusion.

Although stents prevent the processes of arterial recoil and remodeling (transmural vessel shrinkage), which contribute to restenosis following balloon angioplasty, neointimal proliferation inside and/or at the margins of the stented segment have caused recurrent renarrowing in a significant minority of patients. Interestingly, although stents (vs balloon) maximized the initial post-procedural

arterial lumen gain, late lumen loss due to neointimal proliferation elicited by the metal prosthesis was actually greater. Nevertheless, net lumen gain at late follow-up (initial gain – late loss) remained greater following stent deployment. Numerous attempts at reducing neointimal proliferation, and thus, in-stent restenosis with systemically administered adjunctive pharmacotherapies, were unsuccessful. Similarly, the arterial response to injury appeared somewhat stereotyped and was not appreciably influenced by variation in the inciting event (ie laser, atherectomy, balloon, etc). Thus, focus turned toward the basic pathophysiology of arterial injury and its underlying cellular mechanisms.

Greater understanding of the roles of inflammation, cell migration, and proliferation, as well as extracellular matrix deposition, has been gained. More recently, the concept of targeted delivery to the site of arterial injury of medications specifically chosen to inhibit one or more of these processes has been pursued enthusiastically. In addition to the potential for providing high local concentration of medication to suppress the injury response, this concept has the additional attractive attribute of limiting systemic exposure and toxicity.

Although the two US Food and Drug Administration-approved and available drug-eluting stents (DES) differ markedly in metal platform design, polymer, and active pharmacologic agent, their use may be perceived as interchangeable by interventional cardiologists in a manner analogous to "therapeutic substitution" and the concept of "class effect" as applied to pharmacotherapeutics. However, these platforms differ in their net efficacy for suppressing the degree of neointimal proliferative tissue response as measured by quantitative coronary angiography (late loss) or neointimal volume as determined by intravascular ultrasound. One might predict that differences in late coronary lumen loss will be directly related to the subsequent occurrence of adverse clinical events, including restenosis, particularly in smaller vessels. The answer to whether or not appreciable differences in rates of major adverse cardiovascular events can be discerned between the 2 available DES depends on the results of ongoing comparative trials. Furthermore, newer DES systems continue to evolve and include polymer as well as nonpolymer elution strategies, various metal and nonmetal alloy (bioabsorbable) platforms for drug delivery, novel pharmacotherapeutic agents, and/or combinations of all of these theoretical advances.

Finally, as interventional cardiologists, we have largely been forced to extrapolate from data derived from subgroup analyses in lower risk patient cohorts enrolled into pivotal placebo- (or bare metal stent) controlled, randomized comparative trials of DES. Indeed, DES performance in the real world of complex, multi-vessel disease patients, whom we treat in everyday practice, has largely been defined by non-randomized registry experiences. Clearly, we need more data in varied patient subsets to help define appropriate DES utilization.

The current supplement addresses the broad scope of DES issues from basic science mechanisms and proof of concept to angiographic and clinical outcomes in complex patient subsets. Dr. Campbell Rogers provides the unique perspective of a clinical interventionist and basic scientist on the pathophysiology of restenosis as well as differentiating attributes of specific DES platforms. Dr. Emerson Perin takes these issues a step further with respect to incorporating DES pharmacotherapeutic characteristics into the decision-making process for choosing a specific DES. Dr. David Williams examines the safety and efficacy of DES based on an analysis of available randomized controlled trials and registry data. Finally, Drs. Holmes, Simonton, and Kereiakes address the rapidly expanding database of available information on multiple complex patient subsets, including those with small vessels, diabetes, acute myocardial infarction, branch vessel stenosis, and saphenous vein bypass graft target lesions. Novel data sets are presented, which add substantially to our current understanding and comfort in the use of DES in these patient cohorts. The field of coronary intervention with DES is evolving rapidly and the adoption of new DES platforms and new indications for DES utilization should be data driven. Hopefully, the data contained within this supplement will be both valuable and applicable to the clinical practice of interventional cardiologists. ■