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EDITORIAL COMMENT

Bioresorbable Drug-Eluting Stents

No Pain, No Gain*

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Although current-generation metallic-backbone drug-eluting stents are extremely safe and highly efficacious in preventing restenosis, they exhibit a small but steady rate of failure in the years following device implantation (1,2). Recent insights from autopsy and intravascular imaging studies suggest that many of these events are due to an accelerated form of atherosclerosis that develops inside the stent (3). This provides rationale for the development of bioresorbable stents, which break down and disappear once their early scaffolding function has been served.

Two approaches to the development of bioresorbable stents appear most promising. The first approach uses backbones constructed from poly-lactic acid. Two devices leveraging this technology have CE mark approval for use in Europe, the Absorb bioresorbable vascular scaffold (Abbott Vascular, Santa Clara, California) and the DESolve stent (Elixir Medical Corporation, Sunnyvale, California). In addition, the Circulatory System Devices Advisory Panel of the U.S. Food and Drug Administration recently voted to support an application for use of the Absorb stent in the United Sates (4). The second approach uses magnesium stent backbones, which degrade somewhat more rapidly than lactic acid stents. One such device is expected to receive CE mark approval this year (Magmaris, Biotronik, Bülach, Switzerland).

Because of differences in the requirements of regulatory authorities in Europe and the United States, patients and physicians in Europe often have access to novel stent devices prior to the availability of randomized controlled trial data (5). Indeed, bioresorbable stents have been approved for use in Europe for more than 5 years. During this time, data from registries have shown generally favorable results, though evidence suggests a slight increase in the rate of stent thrombosis, especially within the first 30 days after implantation (6-8).

SEE PAGE 1216

In this issue of *JACC: Cardiovascular Interventions*, Sotomi et al. (9) report an interesting analysis from the ABSORB II trial, examining intravascular ultrasound pull backs and quantitative coronary angiography at the time of stent implantation. In this trial, 501 patients were randomly allocated to treatment with bioresorbable Absorb stents or conventional metallic everolimus-eluting stents (EES) (Xience, Abbott Vascular). An interim analysis showed broadly comparable rates of clinical events between the 2 devices at 1 year (10), and primary endpoint results at 3-year follow-up are expected later this year. In the present report, data from 445 patients with intravascular ultrasound imaging pre- and post-intervention were analyzed. The main result was that acute gain (3.46 ± 1.35 mm^2 vs. 4.27 ± 1.46 mm^2; $p < 0.001$) and minimal luminal area after the procedure (5.55 ± 1.46 mm^2 vs. 6.40 ± 1.68 mm^2; $p < 0.001$) were lower with the Absorb stent. This was consistent with the angiographic analysis of this subgroup, as well as with the analysis of the entire treated cohort reported previously (acute gain: 1.15 ± 0.38 mm vs. 1.46 ± 0.38 mm; $p < 0.001$; minimal luminal diameter post-procedure: 2.22 ± 0.33 mm vs. 2.50 ± 0.33 mm; $p < 0.001$) (10). These differences were attributable to differences measured

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immediately after stent implantation; in patients who underwent post-dilation (approximately 60% of all enrolled patients), similar degrees of additional acute gain were seen in both groups.

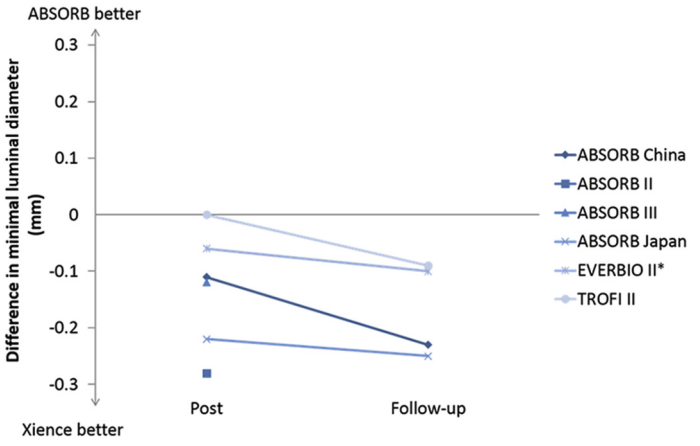
A summary of differences in minimal luminal diameter after the procedure from each of 6 published randomized trials comparing the Absorb stent with metallic EES is shown in **Figure 1** (10–15). The results are broadly consistent across studies, with mean minimal luminal diameter consistently favoring the conventional metallic stent over the Absorb stent. However, the magnitude of difference is relatively small, ranging from a mean difference of 0.00 to 0.28 mm. Moreover, in the trials incorporating planned angiographic follow-up between 6 and 13 months after intervention, the differences in minimal luminal diameter immediately after the procedure seem to contribute importantly to the small differences in antirestenotic efficacy observed between the stents at follow-up (**Figure 1**) (11–14).

These observations are important for 2 reasons. First, randomized trials comparing the Absorb stent with metallic EES show a 2-fold higher rate of stent thrombosis with the Absorb stent and a time-dependent increase in risk that is greatest between 1 and 30 days after stenting (16). Although the reasons for this are likely multifactorial, the observations in relation to differential acute gain provide some mechanistic insight: the degree of residual stenosis in the stented segment is a well-known risk factor for subsequent stent thrombosis (17). Second, the angiographic antirestenotic efficacy of the Absorb stent is marginally inferior to that of metallic EES (16). This analysis suggests that the lower acute gain with the Absorb stent, rather than differences in subsequent late loss, accounts for much of this difference.

In terms of implications for clinical practice, the message seems clear. With current-generation devices, the operator must ensure that every additional effort is made to maximize acute gain with the Absorb stent. This means careful selection of lesions most likely to result in optimal scaffold expansion, meticulous attention to detail with respect to lesion preparation and post-dilation, and liberal use of intravascular imaging to identify and target suboptimal deployment. One practical approach is to use specific implantation protocols to optimize deployment practices. Although this approach is more time consuming and cost intensive, and will not be suitable for every catheterization laboratory, the benefits are likely to be real. Indeed, preliminary observations suggest a detectable improvement in clinical outcomes with such an approach (7).

Finally, at present, the additional pain associated with the implantation of current-generation bioresorbable stents must be borne by the operator. As we look to the future, however, manufacturers will shoulder more of this burden, with iterative development of this still young technology. Ultimately, the availability of new devices with good acute results and similar ease of use to current-generation drug-eluting stents will increase the acceptance of these stents in years to come.

FIGURE 1 Angiographic Outcomes Post-Procedure and at Follow-Up in Patients Randomly Allocated to Treatment With Biodegradable Stents or Metallic Drug-Eluting Stents



Difference in minimal luminal diameter (in-device) between biodegradable stents (Absorb) and metallic drug-eluting stents (Xience) is plotted immediately post-procedure and, if available, at follow-up. Data are derived from published reports of trial data (10–15). *Patients treated with biolimus-eluting stents were not included in the analysis.

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REFERENCES

1. Kimura T, Abe K, Shizuta S, et al. Long-term clinical and angiographic follow-up after coronary stent placement in native coronary arteries. Circulation 2002;105:2986–91.

2. Byrne RA, Iijima R, Mehilli J, et al. Durability of antirestenotic efficacy in drug-eluting stents with and without permanent polymer. J Am Coll Cardiol Intv 2009;2:291–9.

3. Otsuka F, Byrne RA, Yahagi K, et al. Neoatherosclerosis: overview of histopathologic findings and implications for intravascular imaging assessment. Eur Heart J 2015;36:2147–59.

4. Serruys PW. Observations from the recent FDA Circulatory System Devices Panel meeting on bioresorbable vascular scaffolds. EuroIntervention 2016;11:e1569–70.

5. Byrne RA, Serruys PW, Baumbach A, et al. Report of a European Society of Cardiology-European Association of Percutaneous Cardiovascular Interventions Task Force on the Evaluation of Coronary Stents in Europe: executive summary. Eur Heart J 2015;36:2608–20.

6. Capodanno D, Gori T, Nef H, et al. Percutaneous coronary intervention with everolimus-eluting bioresorbable vascular scaffolds in routine clinical practice: early and midterm outcomes from the European multicentre GHOST-EU registry. EuroIntervention 2015;10:1144–53.

7. Puricel S, Cuculi F, Weissner M, et al. Bioresorbable coronary scaffold thrombosis: multicenter comprehensive analysis of clinical presentation, mechanisms, and predictors. J Am Coll Cardiol 2016;67:921–31.

8. Hoppmann P, Kufner S, Cassese S, et al. Angiographic and clinical outcomes of patients treated with everolimus-eluting bioresorbable stents in routine clinical practice: results of the ISAR-ABSORB registry. Catheter Cardiovasc Interv 2016;87:822–9.

9. Sotomi Y, Ishibashi Y, Suwannasom P, et al. Acute gain in minimal lumen area following implantation of everolimus-eluting ABSORB biodegradable vascular scaffolds or Xience metallic stents: intravascular ultrasound assessment from the ABSORB II trial. J Am Coll Cardiol Intv 2016;9:1216–27.

10. Serruys PW, Chevalier B, Dudek D, et al. A bioresorbable everolimus-eluting scaffold versus a metallic everolimus-eluting stent for ischaemic heart disease caused by de-novo native coronary artery lesions (ABSORB II): an interim 1-year analysis of clinical and procedural secondary outcomes from a randomised controlled trial. Lancet 2015;385:43–54.

11. Puricel S, Arroyo D, Corpataux N, et al. Comparison of everolimus- and biolimus-eluting coronary stents with everolimus-eluting bioresorbable vascular scaffolds. J Am Coll Cardiol 2015;65:791–801.

12. Kimura T, Kozuma K, Tanabe K, et al. A randomized trial evaluating everolimus-eluting Absorb bioresorbable scaffolds vs. everolimus-eluting metallic stents in patients with coronary artery disease: ABSORB Japan. Eur Heart J 2015;36:3332–42.

13. Sabate M, Windecker S, Iniguez A, et al. Everolimus-eluting bioresorbable stent vs. durable polymer everolimus-eluting metallic stent in patients with ST-segment elevation myocardial infarction: results of the randomized ABSORB ST-segment elevation myocardial infarction-TROFI II trial. Eur Heart J 2016;37:229–40.

14. Gao R, Yang Y, Han Y, et al. Bioresorbable vascular scaffolds versus metallic stents in patients with coronary artery disease: ABSORB China trial. J Am Coll Cardiol 2015;66:2298–309.

15. Ellis SG, Kereiakes DJ, Metzger DC, et al. Everolimus-eluting bioresorbable scaffolds for coronary artery disease. N Engl J Med 2015;373:1905–15.

16. Cassese S, Byrne RA, Ndrepepa G, et al. Everolimus-eluting bioresorbable vascular scaffolds versus everolimus-eluting metallic stents: a meta-analysis of randomised controlled trials. Lancet 2016;387:537–44.

17. Tada T, Byrne RA, Simunovic I, et al. Risk of stent thrombosis among bare-metal stents, first-generation drug-eluting stents, and second-generation drug-eluting stents: results from a registry of 18,334 patients. J Am Coll Cardiol Intv 2013;6:1267–74.

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