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Bioresorbable Vascular Scaffolds and Very Late Scaffold Thrombosis

Searching an Explanation and a Solution

The recently presented 3-year outcomes of the ABSORB II trial reporting 6 very late scaffold thrombosis (ScT) cases (1) provided a concerning signal regarding current generation bioresorbable vascular scaffolds (BVS).

Prior reports suggested suboptimal implantation including underexpansion and malapposition being the main predisposing factors for ScT, especially up to 1 year, stressing the importance of dedicated implantation techniques. The basic concept of optimal implantation is to obtain "adequate expansion with full apposition." We believed that most ScT events could be prevented if an optimal result is confirmed by intravascular imaging at the end of the procedure. Even with respect to very late ScT, we assumed that full strut apposition would allow sufficient neointimal coverage to prevent intraluminal scaffold dismantling in the later stages of the resorption process.

Several months before the ABSORB II report, 2-year outcomes of the ABSORB Japan trial reported 4 very late ScT cases (2). However, very late ScT did not occur in the subgroup where post-implantation optical coherence tomography was performed, and suboptimal implantation was suspected as the culprit in the ScT cases. Therefore, we believed that it highlighted the importance of post-procedural confirmation with intravascular imaging. By contrast, the 6 very late ScT cases in the ABSORB II trial generate a sense of confusion. Post-procedural intravascular ultrasound was performed in all 6 cases, demonstrating what appears to be adequate strut apposition and scaffold expansion. These findings raise concern regarding whether very late ScT can occur even after obtaining an optimal final result, and whether an unknown scenario might exist during the resorption process.

To our knowledge, the real-world BVS Milan-cohort is unique in that it involves predominantly complex lesions in which a dedicated optimal implantation strategy was consistently used from the first BVS case (3). Following the report of the 3-year ABSORB II data, we urgently updated clinical follow-up, and reviewed the details of all ScT cases including not only definite/probable but also possible ScT cases.

We examined all consecutive lesions treated with Absorb BVS (Abbott Vascular, Santa Clara, California) at 2 high-volume centers in Milan, Italy, between May 2012 and August 2016 (518 lesions with 340 patients). The latest clinical follow-up was performed in November to December 2016 by either clinical visits or telephone interview (clinical follow-up rate, 98.5%). The principles of our BVS implantation strategy have been previously described (3).

Of 518 lesions, most (76%) were type B2 or C as per American College of Cardiology/American Heart Association classification, 46% were bifurcations, the total scaffold length per patient was 54 ± 34 mm, and 45% of patients received at least 1 BVS of 2.5 mm. Pre- (97%) and post-dilation (99.8%) were performed in almost all cases (mean post-dilation pressure was 21 ± 4 atm and the balloon/scaffold ratio was 1.03 ± 0.09). Intravascular imaging was performed in most cases (86%). During the follow-up period (median: 706 days; interquartile range: 355 to 1,088 days), definite or probable ScT was observed in 4 patients (1.2%; 1 acute [Day 0], 1 subacute [Day 3], and 2 late [Day 63 and Day 143]). In contrast, very late definite/probable ScT was not observed. Possible ScT was detected in 5 cases (3 sudden death, 2 unknown death). The details of the cases are shown in Online Table 1. Any cessation of dual antiplatelet therapy was observed in 27.6% of patients until the latest follow-up.

In this update: 1) the occurrence ratio of definite/probable ScT seems acceptable considering the complex lesion subset, and very late ScT was not observed; 2) all definite/probable ScT cases involved a reasonable trigger; and 3) regarding the 5 possible ScT cases detected, we maintain a suspended judgment, although a cause other than ScT seems feasible in all of them.

The problem arising now is that it seems that very late ScT events may have also occurred in cases with acceptable post-procedural results. Despite full strut apposition and an apparent acceptable final result, the lack of consistent high pressure post-dilation in the ABSORB II might have resulted in insufficient embedment into the vessel wall, incomplete endothelialization, and possibly very late events; however, this is merely hypothesis generating.

To further explore this issue, large registries should systematically screen and report updated data regarding ScT.

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Please note: Dr. Latib serves on the advisory board for Medtronic. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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APPENDIX For a supplemental table, please see the online version of this article.

Absorb Bioresorbable Vascular Scaffold Resorption and Imaging Findings

Clarifying Current Misconceptions

The report by Dommasch et al. (1) presents the case of a patient with proximal late focal in-scaffold restenosis 44 months following implantation of 2 Absorb bioresorbable vascular scaffolds (Abbott Vascular, Santa Clara, California). The lesion in the proximal scaffold was successfully treated by implantation of a metallic stent (XIENCE, Abbott Vascular). It is the nomenclature used to describe the imaging findings that requires further clarification.

There have been in recent years several publications describing the in vitro and in vivo behavior of poly-L-lactic acid (PLLA), the structural material of the Absorb bioresorbable vascular scaffold. The degradation of this device follows the typical PLLA behavior curve, which has been well characterized for decades in the published data (2). In the in vivo environment, considering the limited ranges of pH and temperature that are compatible with life, polymer degradation kinetics is controlled by the presence of water alone. Also, PLLA undergoes bulk degradation, meaning that degradation occurs equally throughout the whole material. There are no enzymatic processes and no cellular or inflammatory process involved, given that neither macromolecules nor cells can penetrate the polymer backbone; water alone drives this well-understood hydrolysis reaction. Then, the terms used to describe these imaging findings ("malabsorption and delayed or prolonged resorption") are inaccurate because small-molecular-weight species will continue to form overtime and diffuse away as long as the polymer has access to water with sufficient mobility (i.e., >0°C) to undergo hydrolysis.

The authors observe the presence of transparent boxes by optical coherence tomography at 3.5 years. In vivo degradation studies indicate that by 3 years, PLLA has been fully consumed by hydrolysis, and small-molecular-weight species and monomer have diffused away from the region (3). Furthermore, histological examination of healthy porcine coronary arteries shows that polymer is replaced with provisional matrix with various degrees of cellularity. This was confirmed with polarized light and various histological stains on explanted samples (4). As polymer degrades, extracellular matrix replacement occurs following the architecture of the strut (5). Then, it is not uncommon to identify "strut-like" structures in optical coherence tomography imaging at long term in some of the patients undergoing bioresorbable vascular scaffold implantation. This observation has erroneously led operators to conclude that the polymer has been either "malabsorbed" or it is still present. Thus, the term "malabsorption" (a term borrowed from nutrient transport in the intestine) is an inaccurate description of this phenomenon. The extracellular matrix resulting from polymer resorption is autologous in nature, and thus has a low potential to be thrombogenic or pro-proliferative (5).