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Vasomotor Response to Nitroglycerine Over 5 Years Follow-Up After Everolimus-Eluting Bioresorbable Scaffold Implantation

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ABSTRACT

OBJECTIVES This study investigated the vasomotor response to nitroglycerine (NTG) up to 5 years after ABSORB implantation.

BACKGROUND There are no data regarding long-term vasomotor response after everolimus-eluting bioresorbable vascular scaffold ABSORB implantation.

METHODS We performed quantitative coronary angiography of the scaffolded and proximal and distal adjacent segments of patients from ABSORB Cohort B study before and after 200 μg of intracoronary NTG at 2, 3, and 5 years of follow-up. The mean changes of maximal and mean lumen diameters in the scaffolded and adjacent segments were calculated.

RESULTS The mean in-scaffold lumen diameter change in response to NTG showed a trend to increase over time with absolute values of 0.03 ± 0.09 mm, 0.05 ± 0.12 mm, and 0.07 ± 0.08 mm at 2, 3, and 5 years, respectively ($p = 0.40$). The maximal in-scaffold lumen diameter change significantly increased with values of 0.03 ± 0.14 mm, 0.06 ± 0.16 mm, and 0.11 ± 0.1 mm at 2, 3, and 5 years, respectively ($p = 0.03$). The normalized mean lumen diameter change after NTG in the scaffold relative to the adjacent segments was 51.9 ± 54.8% at 5 years of follow-up ($p = 0.60$).

CONCLUSIONS Although there was a numerical increase of the vasomotor response to NTG after ABSORB implantation measured by quantitative coronary angiography with mean lumen diameter, the change was not statistically significant. However, the maximal lumen diameter changes increased over time from 2 to 5 years and attained statistical significance. The vasomotor response to NTG after ABSORB implantation moderately trended to increase, which is consistent with the progressive degradation and bioresorption of the scaffold, but the degree of vasomotor response remained lower in comparison with adjacent segments. (J Am Coll Cardiol Intv 2017;10:786–95) © 2017 by the American College of Cardiology Foundation.

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At the 1-year follow-up of patients in the ABSORB Cohort B2, tests with different stimuli (acetylcholine or methergine) showed the return of vasomotion function (1). After endothelial-dependent stimulation with acetylcholine, a vasodilatory response was observed in 30% of patients, suggesting recovery of normal endothelial function (1). The recovery of vasomotion was correlated with signs of bioresorption as a reduction of hyperechogenicity assessed with intravascular ultrasound (IVUS) examination (2). At the 2-year follow-up among a small analyzable group of patients from Cohort A (using ABSORB 1.0), the response to nitroglycerine (NTG) and acetylcholine was even greater than at 1 year as seen in Cohort B2 and almost 50% of patients showed recovery of endothelial function (1). Although these observations were made in separate cohorts of patients who had different versions of the device implanted, it was confirmed that, during the resorption process, the mechanical integrity of the scaffold is lost as expected. The vessel, freed from a constraining scaffold, seemed to respond again to vasomotor stimulation. However, most recently the ABSORB-II study did not meet its co-primary endpoint of superior vasomotor reactivity of the ABSORB scaffold in comparison to the Xience V stent after 3 years (3),

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In ABSORB II at 3 years, ABSORB demonstrated vasomotion consistent with previous evidence, such as ABSORB Cohort B. The reason for not showing superiority over Xience in ABSORB II was that XIENCE unexpectedly showed some movement contrary to historical data with older generation metallic stents. Angiography may not be the most appropriate methodology for assessing differences in vasomotion. The revised platform of the scaffold (ABSORB bioresorbable vascular scaffold Rev.1.1) has a prolonged bioresorption process with a loss of structural scaffold integrity between 6 and 12 months and complete resorption at approximately 3 years (4). The aim of the current study was to examine the vasomotility up to 5 years after implantation of the Conformité Européenne marked and commercially available ABSORB bioresorbable vascular scaffold (ABSORB bioresorbable vascular scaffold Rev.1.1) in Cohort B as measured by the endothelial-independent, NTG-induced vasomotion (5).

METHODS

STUDY POPULATION. The ABSORB Cohort B trial (A Clinical Evaluation of the Bioresorbable Everolimus-Eluting Coronary Stent System in the Treatment of Patients with de Novo Native Coronary Artery Lesions) is a multicenter, single-arm, unblinded trial evaluating the safety and feasibility of the ABSORB bioresorbable vascular scaffold 3.0 × 18 mm in the treatment of patients with up to 2 de novo coronary lesions with diameter of 3.0 mm and length of <14 mm in native coronary arteries. A total of 101 patients enrolled in the trial were randomly assigned to group B1 (n = 45) with invasive follow-up at 6 and 24 months or group B2 (n = 56) with control imaging procedures at 12 and 36 months. All patients were requested, according to a protocol amendment, to undergo invasive imaging follow-up at 5 years.

ABBREVIATIONS AND ACRONYMS

IVUS = intravascular ultrasound

NTG = nitroglycerine

QCA = quantitative coronary angiography

The ABSORB study was sponsored by Abbott Vascular. The study protocol was approved by the ethics committee at the participating institutions and the patients gave written informed consent before inclusion.

ANGIOGRAPHIC ASSESSMENT AND VASOMOTION TEST WITH NTG. Oral nitrates, β-blockers, and calcium channel blockers were to be stopped at least 12 h before the coronary angiography and vasomotion test procedure. Vasomotion response in group B1 and B2 patients was tested at 2, 3, and 5 years by injecting 200 μg intracoronary NTG. In the present paper, to assess endothelial independent vasomotory reaction without the potential influence of other vasoactive stimulation, the angiographic results of the tests performed only with NTG at 2, 3, and 5 years of follow-up are presented. Quantitative coronary angiography (QCA) analysis of the scaffolded segment (determined as the length between the radiopaque platinum markers at both ends of the ABSORB bioresorbable vascular scaffold) as well as 5-mm adjacent to the proximal and distal segments was performed. The same matching projections were used for the 2-, 3-, and 5-year vasomotion analysis. The absolute (mm) difference of maximal and mean lumen diameter before and after the administration of NTG was measured in the scaffold as well as in the adjacent reference segments. A normalized change in mean lumen diameter (in percent) of the scaffolded segment relative to the reference segments was calculated as:

$$\%\ \text{normalized mean lumen diameter change} = \frac{\textit{in scaffold Mean LD change}}{(\textit{prox mean LD change} + \textit{distal Mean LD}) \div 2} \times 100\%$$

The QCA analyses with the CAAS II software (Pie Medical, Maastricht, the Netherlands), were performed by an independent Core Laboratory (Cardialysis, Rotterdam, the Netherlands).