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Relation Between Bioresorbable Scaffold Sizing Using QCA-Dmax and Clinical Outcomes at 1 Year in 1,232 Patients From 3 Study Cohorts (ABSORB Cohort B, ABSORB EXTEND, and ABSORB II)

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ABSTRACT

OBJECTIVES This study sought to investigate the clinical outcomes based on the assessment of quantitative coronary angiography–maximal lumen diameter (Dmax).

BACKGROUND Assessment of pre-procedural Dmax of proximal and distal sites has been used for Absorb scaffold size selection in the ABSORB studies.

METHODS A total of 1,248 patients received Absorb scaffolds in the ABSORB Cohort B (ABSORB Clinical Investigation, Cohort B) study (N = 101), ABSORB EXTEND (ABSORB EXTEND Clinical Investigation) study (N = 812), and ABSORB II (ABSORB II Randomized Controlled Trial) trial (N = 335). The incidence of major adverse cardiac events (MACE) (a composite of cardiac death, any myocardial infarction [MI], and ischemia-driven target lesion revascularization) was analyzed according to the Dmax subclassification of scaffold oversize group versus scaffold nonoversize group.

RESULTS Of 1,248 patients, pre-procedural Dmax was assessed in 1,232 patients (98.7%). In 649 (52.7%) patients, both proximal and distal Dmax values were smaller than the nominal size of the implanted scaffold (scaffold oversize group), whereas in 583 (47.3%) of patients, the proximal and/or distal Dmax were larger than the implanted scaffold (scaffold nonoversize group). The rates of MACE and MI at 1 year were significantly higher in the scaffold oversize group than in the scaffold nonoversize group (MACE 6.6% vs. 3.3%; log-rank $p < 0.01$, all MI: 4.6% vs. 2.4%; log-rank $p = 0.04$), mainly driven by a higher MI rate within 1 month post-procedure (3.5% vs. 1.9%; $p = 0.08$). The independent MACE determinants were both Dmax smaller than the scaffold nominal size (odds ratio [OR]: 2.13, 95% confidence interval [CI]: 1.22 to 3.70; $p < 0.01$) and the implantation of overlapping scaffolds (OR: 2.10, 95% CI: 1.17 to 3.80; $p = 0.01$).

CONCLUSIONS Implantation of an oversized Absorb scaffold in a relatively small vessel appears to be associated with a higher 1-year MACE rate driven by more frequent early MI. (ABSORB Clinical Investigation, Cohort B [ABSORB Cohort B], NCT00856856; ABSORB EXTEND Clinical Investigation [ABSORB EXTEND], NCT01023789; ABSORB II Randomized Controlled Trial [ABSORB II], NCT01425281) (J Am Coll Cardiol Intv 2015;8:1715–26) © 2015 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

Dmax = maximal lumen diameter

ID = ischemia-driven

MACE = major adverse cardiac event(s)

MI = myocardial infarction

MLD = minimal lumen diameter

OCT = optical coherence tomography

PMI = periprocedural myocardial infarction

QCA = quantitative coronary angiography

OR = odds ratio

ST = scaffold thrombosis

TLR = target lesion revascularization

TVMI = target vessel myocardial infarction

QCA = quantitative coronary angiography

The performance of the second-generation Absorb bioresorbable everolimus-eluting scaffold was investigated in the ABSORB II (ABSORB II Randomized Controlled Trial) as well as in the Cohort B1, Cohort B2, and ABSORB EXTEND (ABSORB EXTEND Clinical Investigation) studies, and demonstrated excellent clinical results (1–7). As the Absorb scaffold has a strict upper limit of expansion, quantitative coronary angiography (QCA)-guided implantation was a mandatory requirement in ABSORB EXTEND (7) and ABSORB II (1). The aim was to allow the selection of a scaffold size matching that of the reference vessel diameter. For reasons related to the potential labeling by the regulator, the sponsoring corporation did not want to require the use of intravascular imaging for sizing the vessel and for selection of the device size. The concerns about appropriate deployment of the Absorb scaffold with angiography guidance arose mainly from optical coherence tomography (OCT) substudies demonstrating an increased frequency of malapposition when the Absorb scaffold was implanted in a too large vessel (8). Another matter of concern is the risk of scaffold disruption (9), particularly when the device has already reached its maximal limit of expansion and is overexpanded in an attempt to correct persistent malapposition. Conversely, an OCT substudy showed an excess of proximal and/or distal edge dissections when the Absorb scaffold was implanted in vessels smaller than the device nominal size (8). However, the impact of quantitative angiographic guidance on clinical outcomes is so far unknown. Therefore, the aim of this study was to investigate the relationship between clinical outcomes and maximal diameter (Dmax) by QCA, which was used as a guide for appropriate selection and deployment of the Absorb scaffold in 2 cohorts of patients from the ABSORB Cohort B study, ABSORB EXTEND study, and ABSORB II trial.

METHODS

STUDY DESIGN AND POPULATION. We analyzed the results of Absorb scaffold implantation in 1,248 patients enrolled between 2009 and 2013 in the ABSORB Cohort B study (2,4), ABSORB EXTEND study (7), and ABSORB II (1) randomized controlled trial. The design of each study is described elsewhere (4,6,7,10). In the ABSORB Cohort B, a 3.0 × 18-mm Absorb scaffold only was available. In the ABSORB EXTEND and ABSORB II studies, patients were treated as follows (1,7): 1) a 3.5-mm Absorb scaffold was used when both the proximal and distal Dmax were within an upper limit of 3.8 mm and a lower limit of 3.0 mm: 2) a 3.0-mm Absorb scaffold was used when both the proximal and distal maximal lumen diameters were within an upper limit of 3.3 mm and a lower limit of 2.5 mm: 3) a 2.5-mm Absorb scaffold was used when both the proximal and the distal Dmax were within an upper limit of 3.0 mm and a lower limit of 2.25 mm: and 4) scaffold overlap was allowed. Patients demographic data and baseline characteristics were similar among 3 studies as well as pre-procedure minimal lumen diameter (MLD) and % diameter stenosis. All of these trials were sponsored and funded by Abbott Vascular. The research ethics committee of each participating institution approved the protocol, and all enrolled patients provided written informed consent before inclusion.

STUDY DEVICE. The details of the study device (Absorb, Abbott Vascular, Santa Clara, California) have been described in detail previously (5,6). In brief, the balloon-expandable Absorb scaffold comprises a poly-L-lactide backbone (6) coated with an amorphous drug-eluting coating matrix composed of poly-D,L-lactide polymer containing everolimus.

QCA ANALYSIS. QCA guidance of Absorb implantation relies on the angiographic diameter function curve of the pre-treatment vessel segment that contains 3 nonambiguous data points; namely, the MLD and the Dmax with respect to the MLD of the proximal (proximal Dmax) and distal (distal Dmax) vessel segments of interest (8,11) (**Figure 1**). QCA analyses were undertaken by the sites before Absorb implantation, and post-procedurally by an independent core laboratory (Cardialysis BV, Rotterdam, the Netherlands) using a Coronary Angiography Analysis System (Pie Medical Imaging, Maastricht, the Netherlands).

DEFINITIONS AND ENDPOINTS. The patient population in the present study was stratified by the difference between the angiographic maximal diameter

employees of Abbott Vascular. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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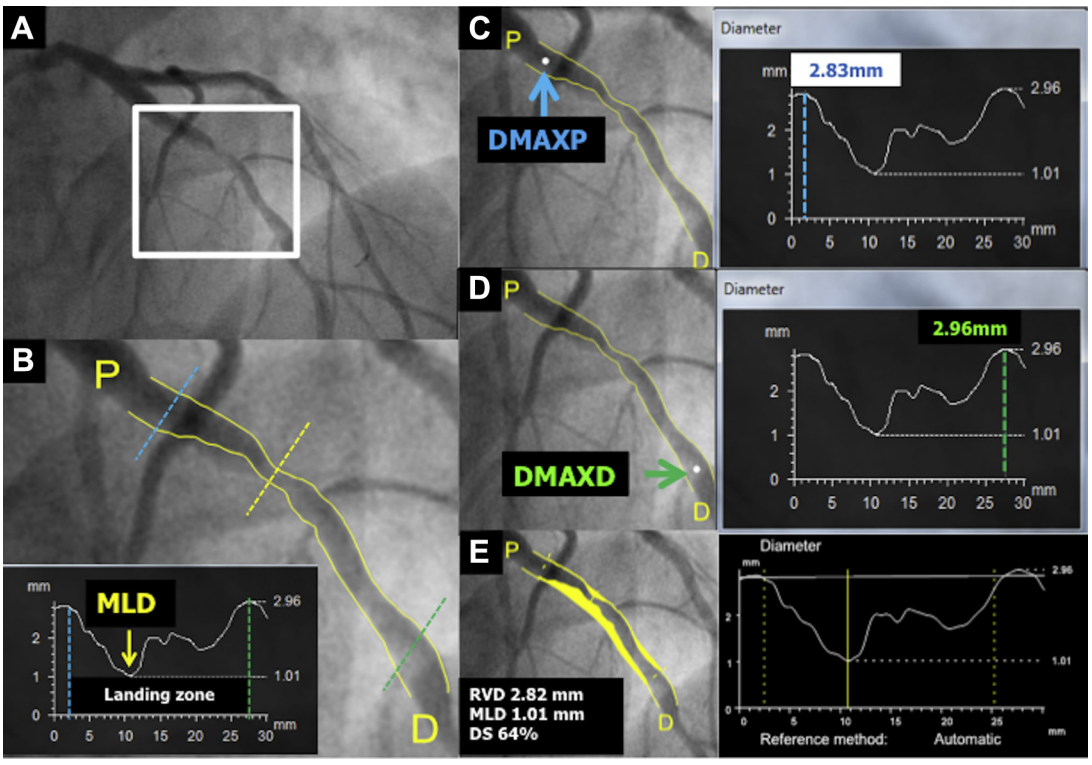
FIGURE 1 The Method to Measure QCA Proximal and Distal Dmax

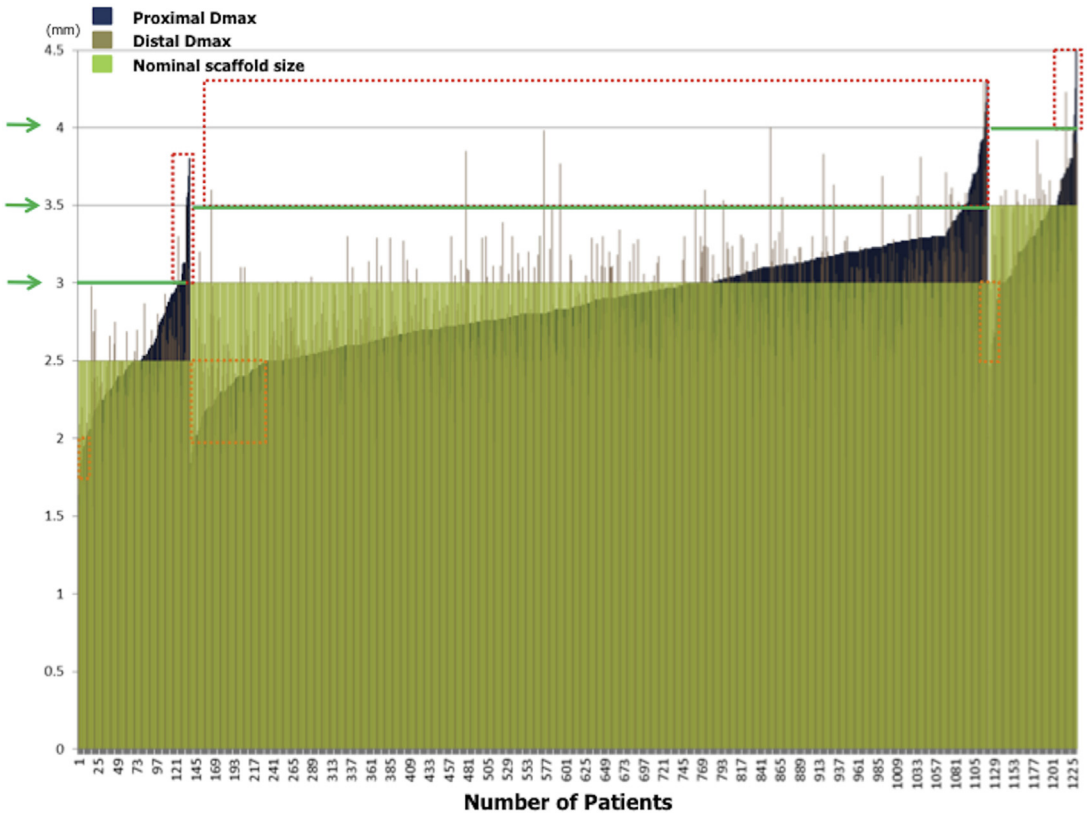


The method used to measure proximal and distal Dmax with QCA is shown. In the pre-procedural angiography **(A)**, the operator has to define the landing zone where the scaffold will be implanted **(B)**. Within the landing zone, the peak of the diameter function curve proximal to the minimal lumen diameter is defined as proximal (P) Dmax **(C)**, whereas the peak diameter function curve distal **(D)** to the minimal lumen diameter is defined as distal Dmax **(D)**. In this case, the proximal and distal Dmax of 2.83 and 2.96 mm led to the correct sizing of the Absorb (3.0 mm) with regard to the vessel diameter **(E)**. DMAXD = maximal lumen diameter distal; DMAXP = maximal lumen diameter proximal; MLD = minimal lumen diameter; QCA = quantitative coronary angiography; RVD = reference vessel diameter.

and the nominal diameter of the implanted scaffold. The selection of device size was considered "oversized" (scaffold oversize group) when the patient received 1 or more devices in vessels in which both the proximal and the distal Dmax were smaller than the nominal size of the device. Patients who received Absorb scaffolds in vessels with either a proximal or a distal Dmax or both Dmax larger than the nominal size of the device constituted the "scaffold nonoversize group". When a patient received 2 or 3 overlapping Absorb scaffolds in a long lesion, the nominal size of the proximally implanted device was compared with the proximal Dmax, whereas the nominal size of the distally implanted device was compared with the distal Dmax. In the cases of device failure (n = 10), the difference between Dmax and the implanted metallic stent was calculated. An additional analysis was performed using a different criterion (nominal scaffold diameter within 0.4 or 0.5 mm of Dmax) and is presented in Online Tables 1 and 2.

In the present analysis, the primary clinical outcome assessed was ischemia-driven major adverse cardiac events (ID-MACE), defined as a composite of cardiac death, any myocardial infarction (MI classified as Q-wave or non-Q-wave MI), and ischemia-driven target lesion revascularization (ID-TLR) by coronary artery bypass graft or percutaneous coronary intervention. Cardiac death was defined as any death due to a proximate cardiac cause (e.g., MI, low-output failure, fatal arrhythmia). Unwitnessed death and death of unknown cause were classified as cardiac death. MI classification and criteria for diagnosis were defined according to the per-protocol definition. Q-wave MI was the development of a new, pathological Q-wave. Non-Q-wave MI was adjudicated if there was an elevation of CK levels to ≥2 times the upper limit of normal with

FIGURE 2 Proximal and Distal Dmax Compared With Nominal Size of the Scaffold



The graph represents the proximal Dmax value, the distal Dmax value and the nominal size of the implanted Absorb scaffold(s) in 1,232 patients. The Dmax measurement is based on core lab assessment. According to the manufacturer, the 2.5-mm, 3.0-mm, and 3.5-mm scaffolds cannot be dilated beyond their nominal size of 3.0 mm, 3.5 mm, and 4.0 mm, respectively. The limit of expansion of the scaffold is depicted by a **green continuous line**. Theoretically, **dotted red areas** indicate implantation of a too "small" Absorb scaffold in a relatively large vessel, and **dotted orange areas** indicate implantation of a too "large" Absorb scaffold in a relatively small vessel. Device size selection with regard to Dmax was considered appropriate in 867 (70.4%) patients and inappropriate in 365 (29.6%) patients. Dmax = maximal lumen diameter.

elevated creatine kinase-myocardial band levels in the absence of new pathological Q waves (12). Notably, this definition of per-protocol MI was consistently applied in all trials included in the present analysis. Target vessel myocardial infarction (TVMI) was defined as MI that occurred in the entire major coronary vessel proximal and distal to the target lesion, which includes upstream and downstream branches and the target lesion itself. ID-TLR was defined as any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel with either a positive functional ischemia study, ischemic symptoms, or an angiographic MLD stenosis ≥50% by core laboratory QCA, or revascularization of a target lesion with diameter stenosis ≥70% by core laboratory QCA without either ischemic symptoms or a positive functional study. Definite and probable scaffold thrombosis (ST) was adjudicated according to the Academic Research Consortium definitions (13–15). All clinical outcomes were adjudicated by an independent clinical events committee.

SOURCE DOCUMENT VERIFICATION AND CLINICAL FOLLOW-UP. In the ABSORB Cohort B and ABSORB II studies, we verified source documents in 100% of patients through 1-year follow-up. In the ABSORB EXTEND trial, source document verification was routinely performed in 100% of patients through 30-day follow-up, subsequently in a random 20% of patients, and in 100% of all reported events for the remaining follow-up period.

STATISTICAL ANALYSIS. All analyses were conducted using the intention-to-treat population. For the

present analyses, individual data were based on a patient-level basis. Categorical variables were compared by Fisher exact test. Continuous variables are presented as mean ± SD and were compared by nonparametric test. Time-to-event variables are presented as Kaplan-Meier curves. To determine the independent predictors of MACE, firstly univariate logistic regression models were constructed using the following variables: age, male sex, current smoking, hypertension requiring treatment, dyslipidemia requiring treatment, any diabetes, unstable angina, pre-procedural diameter stenosis, pre-procedural MLD, lesion length, angulation >45°, bifurcation lesions, calcified lesions, pre-procedural visible thrombus, Type B2/C lesions, target vessel treatment with 2.5-mm device, treatment with overlapping scaffolds, and scaffold implantation in a vessel with both proximal and distal Dmax smaller than the nominal device size. Secondly, significant variables ($p < 0.10$) in the univariate analysis were forcedly entered into a multivariable logistic regression model to predict for MACE. A 2-sided p value <0.05 was considered significant for all tests. All statistical tests were performed with SPSS, version 22.0 for windows (IBM, Chicago, Illinois).

RESULTS

Of a total population of 1,248 patients, pre-procedural Dmax was assessed by the core laboratory in 1,232 (98.7 %) patients. **Figure 2** displays individual values of proximal and distal Dmax in patients who received Absorb scaffolds of either 2.5-mm, 3.0-mm, or 3.5-mm nominal size. The nominal size of the implanted Absorb scaffold was larger than both proximal and distal Dmax in 649 patients (scaffold oversize group 52.7%).

Clinical and angiographic characteristics between the scaffold oversize group and the scaffold nonoversize group are detailed in **Table 1**. The 2 groups did not significantly differ with regard to main baseline clinical characteristics, whereas pre-procedural MLD, reference vessel diameter, and both proximal and distal Dmax were significantly smaller in the scaffold oversize group than in the scaffold nonoversize group.

The scaffold oversize group was associated with a higher risk of ID-MACE than the scaffold nonoversize group. As illustrated in **Figure 3**, the graphical presentation clearly shows that a higher number of these patients can be seen in the lower left quadrant (scaffold oversize group) than in the other quadrants of the graph (6.6% vs. 3.3%, $p < 0.01$). MACE occurred in 46 of 760 patients when a relatively large device size was selected, whereas it occurred in 16 of 472 patients when a relatively small device size was selected (6.1% vs. 3.4%, $p = 0.04$).

The MACE and MI rates at 1 year and 2 years were significantly higher in the scaffold oversize group

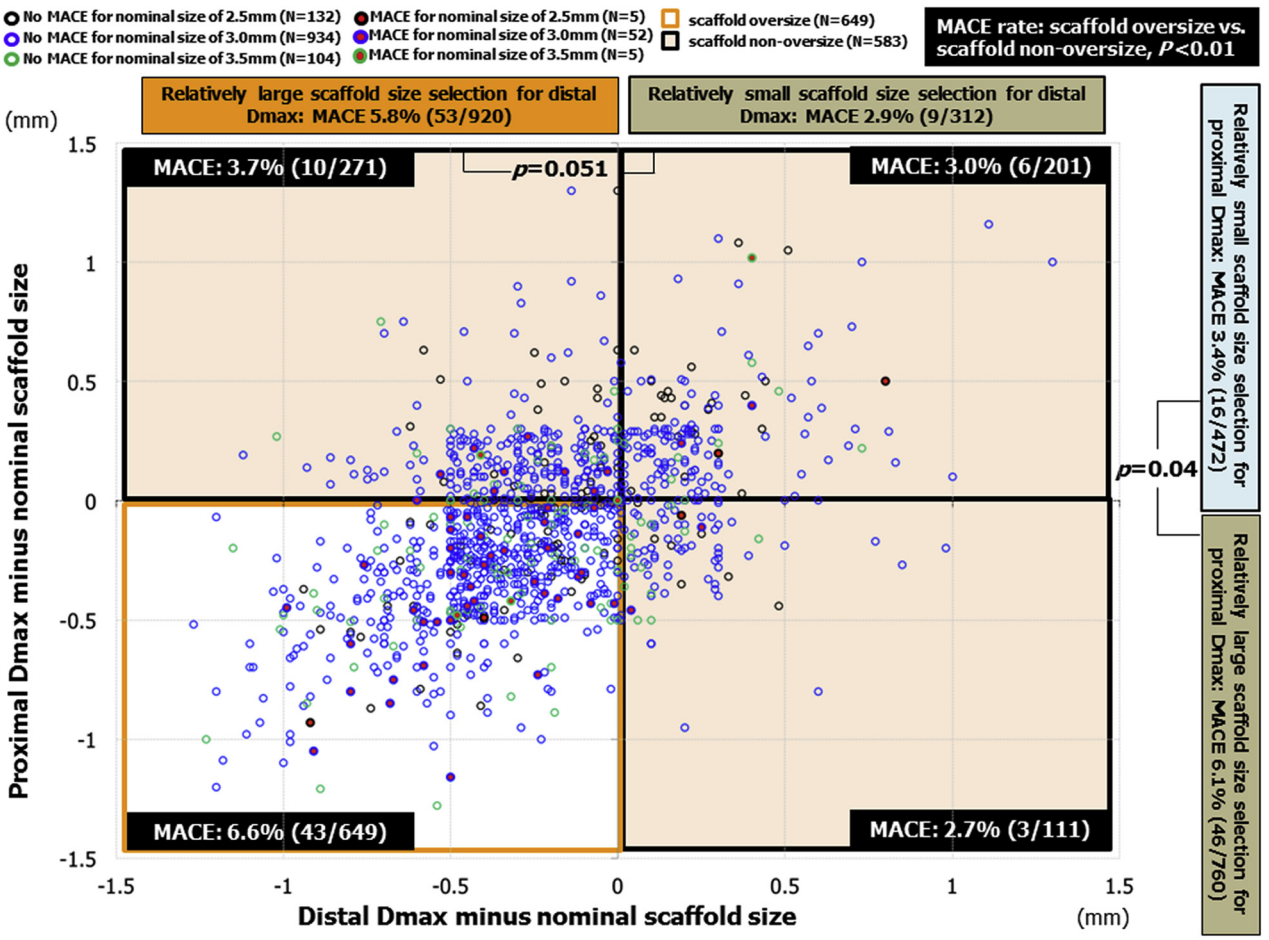
TABLE 1 Clinical and Pre- and Post-Procedural Angiographic Characteristics

	Scaffold Oversize Group (n = 649)	Scaffold Nonoversize Group (n = 583)	p Value
Age, yrs	61.6 ± 10.7	60.8 ± 10.1	0.20
Male	73.8 (479)	75.1 (438)	0.60
Current smoker	1.7 (141)	24 (140)	0.34
Hypertension requiring treatment	67.6 (439)	67.9 (396)	0.95
Dyslipidemia requiring treatment	69.8 (453)	69 (402)	0.76
Any diabetes mellitus	24 (156)	26.2 (153)	0.39
Unstable angina	24.8 (161)	22.9 (133)	0.46
Prior history of myocardial infarction	28.1 (182)	27.8 (162)	0.95
Lesion location			
Right coronary artery	21.9 (142)	33.6 (196)	<0.01
Left anterior descending artery	49.8 (323)	41.9 (244)	0.01
Left circumflex artery or ramus	9.9 (64)	9.6 (56)	0.92
Left main coronary artery	0 (0)	0.2 (1)	0.47
ACC/AHA lesion complexity			
A	1.9 (12)	2.1 (12)	0.84
B1	53.9 (349)	52.8 (307)	0.73
B2	41.2 (267)	43.5 (25)	0.45
C	3.1 (20)	1.7 (10)	0.14
TIMI flow grade 0 or 1	0.6 (4)	0.2 (1)	0.38
Calcification (moderate or severe)	13.4 (87)	14.4 (84)	0.62
Angulation ≥45°	2.6 (17)	2.2 (13)	0.71
Bifurcation	4.0 (26)	4.8 (28)	0.58
Thrombus	1.5 (10)	1.9 (11)	0.67
Pre-procedural			
Reference vessel diameter, mm	2.50 ± 0.33	2.79 ± 0.39	<0.01
Proximal Dmax, mm	2.66 ± 0.30	3.11 ± 0.34	<0.01
Distal Dmax, mm	2.58 ± 0.31	2.94 ± 0.38	<0.01
Minimal lumen diameter, mm	1.05 ± 0.30	1.15 ± 0.33	<0.01
Diameter stenosis, %	57.9 ± 10.9	58.6 ± 10.2	0.22
Obstruction lesion length, mm	12.2 ± 5.9	13.0 ± 5.7	0.03
Device related			
2.5-mm scaffold	8.6 (56)	13.9 (81)	<0.01
3.0-mm scaffold	82.4 (535)	77.4 (451)	0.03
3.5-mm scaffold	8.9 (58)	8.8 (51)	0.92
Average nominal diameter	2.97 ± 0.24	3.00 ± 0.21	0.03
Post-procedural			
Reference vessel diameter, mm	2.58 ± 0.30	2.82 ± 0.34	<0.01
Minimal lumen diameter, mm	2.19 ± 0.28	2.37 ± 0.31	<0.01
Diameter stenosis, %	15.3 ± 6.5	15.9 ± 10.2	0.09
Acute decrease, % diameter stenosis	42.5 ± 12.5	42.5 ± 12.4	0.98
Acute gain, mm	1.13 ± 0.34	1.21 ± 0.38	<0.01
Acute gain/pre-procedural RVD, mm	0.46 ± 0.14	0.44 ± 0.14	0.02
Bailout treatment with metallic stent	1.9 (12)	0.7 (4)	0.08

Values are mean ± SD, or % (n). Clinical and pre- and post-procedural angiographic characteristics are according to the distribution of Dmax measurements minus the nominal scaffold size in the scaffold oversize group versus the scaffold nonoversize group.

ACC/AHA = American College of Cardiology/American Heart Association lesion characteristics; Dmax = maximal lumen diameter; RVD = reference vessel diameter; TIMI = Thrombolysis In Myocardial Infarction.

FIGURE 3 Distribution of the Difference Between Dmax and Nominal Scaffold

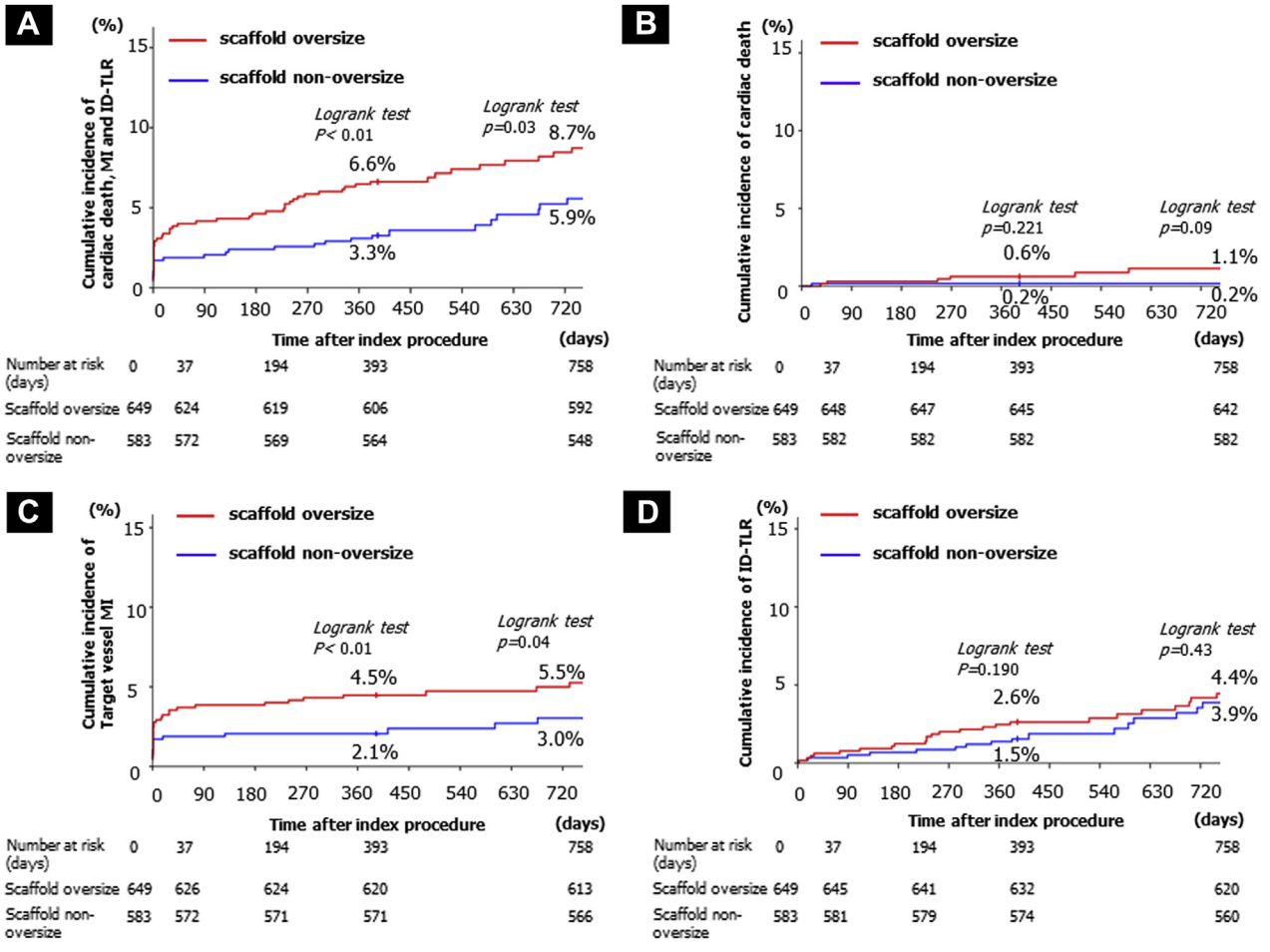


Distribution of proximal and distal Dmax measurements minus nominal scaffold size in patients with or without major adverse cardiac events is shown. When the appropriateness of scaffold size was defined by nominal scaffold diameter within 0.5 mm of Dmax, the differences between the distal Dmax and nominal scaffold size are plotted on the y-axis and x-axis, respectively. The **red filled circles** represent the patients who experienced ID-MACE at 1 year. The graphical presentation demonstrates that major adverse cardiac events (MACE) were more frequently observed in patients in whom both proximal and distal Dmax were smaller than the device nominal size (6.6% vs. 3.3%, $p < 0.01$) **(lower left quadrant)**. Dmax = maximal lumen diameter; ID-MACE = ischemia-driven major adverse cardiac event(s).

than in scaffold nonoversize group (1-year MACE: 6.6% vs. 3.3%; log-rank $p < 0.01$, 2-year MACE: 8.7% vs. 5.9%; log-rank $p = 0.03$, 1-year TVMI: 4.5% vs. 2.1%, 2-year MI: 5.5% vs. 3.0%; log-rank $p = 0.04$), mainly driven by a higher rate of TVMI within 1 month after the procedure (3.5% vs. 1.9%; $p = 0.08$) (Figure 4, Tables 2 and 3). Among the events of MI (44 of 1,232), periprocedural MI (PMI) occurred in 28 cases (63.6%). MI occurred after 48 h in 36% of all MI events. In the scaffold oversize group, PMI occurred in 64% (18 cases), whereas in the scaffold nonoversize group, the PMI rate was 35.7% (10 cases). There were no statistically significant differences in the incidence of overall angiographic complications that could be documented at the end of the procedure for patients who had TVMI within 1 month (3.1% vs. 1.7%; $p = 0.14$) (Table 3). The incidence of ST tended to be higher in the scaffold oversize group than in the scaffold nonoversize group (Table 2) (1.54% vs. 0.51%, OR: 3.03 [0.83 to 11.05]; $p = 0.10$). The acute definite ST rate was 0.15% and 0% in the scaffold oversize group and the scaffold nonoversize group, respectively ($p = 1.0$). Subacute and late definite ST were not significantly different among the 2 groups (Online Table 3). A case of a definite early ST is shown in Figure 5.

When the appropriateness of scaffold size was defined by nominal scaffold diameter within 0.5 mm

FIGURE 4 Time-to-Event Curves of MACE and Its Components



Time-to-event curves of MACE **(A)** and its components (**B**: death, **C**: target vessel MI; **D**: ID-TLR) at 2 years, according to study group. ID-TLR = ischemia-driven target lesion revascularization; MACE = major adverse cardiac event(s); MI = myocardial infarction.

of Dmax, there was no statistically significant difference in MACE between the 2 groups, (appropriate 4.5% vs. inappropriate 6.3%; p = 0.20). When the cutoff of 0.4 mm is used, there was a significant difference in MACE between appropriate and inappropriate scaffold deployment (3.4% vs. 6.8%; p = 0.006) (Online Figures 1 and 2, Online Table 3).

INDEPENDENT PREDICTOR OF MACE AFTER IMPLANTATION OF ABSORB SCAFFOLD(S). With multivariable logistic regression analysis, the independent determinants of 1-year MACE were: implantation of the Absorb scaffold(s) in a vessel with both proximal and distal Dmax smaller than the device nominal size (OR: 2.13, 95% CI: 1.22 to 3.70; p < 0.01) and overlapping scaffolds (OR: 2.10, 95% CI: 1.17 to 3.80; p = 0.01) (Table 4).

DISCUSSION

The main findings of this study are: 1) 52.7% (n = 649) of patients had an "oversize" scaffold implantation; 2) The MACE and MI rates at 1 year were significantly higher in the scaffold oversize group than in the scaffold nonoversize group (MACE: 6.6% vs. 3.3%, log-rank p < 0.01, all MI: 4.6% vs. 2.4%; log-rank p = 0.04), mainly driven by a higher rate of MI within 1 month after the procedure (3.5% vs. 1.9%; p = 0.08); the incidence of definite ST tended to be higher in the scaffold oversize group than in the scaffold nonoversize group (1.54% vs. 0.51%,OR: 3.03 [0.83 to 11.05]; p = 0.10); 3) The independent determinants of MACE were both Dmax smaller than the device nominal size (OR: 2.13, 95% CI: 1.22 to 3.70;

TABLE 2 Incidence of Clinical Events at 1 Year

Clinical Outcomes	Scaffold Oversize Group (n = 649)		Scaffold Nonoversize Group (n = 583)		OR [95% CI]	p Value
	% (n)	95% CI	% (n)	95% CI		
Cardiac death	0.62 (4)	0.17–1.57	0.17 (1)	0.00–0.95	3.61 (0.40–32.39)	0.38
Myocardial infarction	4.62 (30)	3.14–5.53	2.40 (14)	1.32–4.00	1.97 (1.03–3.75)	0.049
QMI	1.23 (8)	0.53–2.41	0.34 (2)	0.04–1.23	3.63 (0.77–17.14)	0.11
NQMI	3.39 (22)	2.14–5.09	2.06 (12)	1.07–3.57	1.67 (0.82–3.40)	0.17
TVMI	4.47 (29)	3.01–6.35	2.06 (12)	1.07–3.57	2.23 (1.13–4.40)	0.025
Ischemia-driven TLR	2.62 (17)	1.53–4.16	1.54 (9)	0.71–2.91	1.72 (0.76–3.88)	0.23
Composite of cardiac death, all MI, and clinically indicated target lesion revascularization (MACE)	6.63 (43)	4.84–8.82	3.26 (19)	1.97–5.04	2.11 (1.21–3.66)	<0.01
Composite of cardiac death, target vessel MI, and clinically indicated target lesion revascularization (DoCE)	6.32 (41)	4.57–8.47	2.92 (17)	1.71–4.63	2.25 (1.26–3.99)	<0.01
Composite of all death, all MI, and all revascularization (PoCE)	8.01 (52)	6.04–10.37	4.46 (26)	2.93–6.47	1.87 (1.15–3.03)	0.01
Scaffold thrombosis	1.54 (10)	0.74–2.82	0.51 (3)	0.11–1.50	3.03 (0.83–11.05)	0.10
Definite ST	0.92 (6)	0.34–2.00	0.51 (3)	0.11–1.50	1.80 (0.45–7.25)	0.51
Probable ST	0.31 (2)	0.04–1.11	0 (0)	0.00–1.01	NA	1.0
Possible ST	0.31 (2)	0.04–1.11	0 (0)	0.00–1.01	NA	1.0

Incidence of clinical events at 1 year are according to the distribution of Dmax measurements minus the nominal scaffold size in the scaffold oversize group versus the scaffold nonoversize group.

CI = confidence interval; Dmax = maximal lumen diameter; DoCE = device-oriented composite endpoint; MACE = major adverse cardiac event(s); MI = myocardial infarction; NQMI = non-Q-wave myocardial infarction; OR = odds ratio; PoCE = patient-oriented composite endpoint; QMI = Q-wave myocardial infarction; ST = scaffold thrombosis; TLR = target lesion revascularization; TVMI = target vessel myocardial infarction.

$p < 0.01$) and overlapping scaffolds (OR: 2.10, 95% CI: 1.17 to 3.80; $p = 0.01$).

As illustrated in the scaffold oversize group in Figure 3, proximal and distal Dmax were significantly smaller than in the scaffold nonoversize group (proximal Dmax: 2.66 ± 0.30 mm vs. 3.11 ± 0.34 mm; $p < 0.01$, distal Dmax: 2.58 ± 0.31 mm vs. 2.94 ± 0.38 mm; $p < 0.01$, respectively) (Table 1). In the population described in the scaffold oversize group, 2.5-mm device size scaffolds were less frequently selected (8.6% vs. 13.9%; $p < 0.01$) as compared with 3.0-mm scaffolds (82.4% vs. 77.4%; $p = 0.03$). In the scaffold oversize group, acute gain normalized for preprocedural reference vessel diameter was higher (0.46 ± 0.14 vs. 0.44 ± 0.14; $p = 0.02$) and bailout treatment with metallic stents was more frequently performed (1.9% vs. 0.7%; $p = 0.08$) compared with the nonoversize group (Table 1). Implanting Absorb scaffold(s) in a vessel with both proximal and distal Dmax smaller than the device nominal size may cause edge dissections due to the higher balloon/device-artery ratio during scaffold deployment.

TABLE 3 Incidence of TVMI

	Scaffold Oversize Group (n = 649)	Scaffold Nonoversize Group (n = 583)	p Value
TVMI at 12 months after index procedure	4.5 (29)	2.1(12)	0.025
TVMI within 1 month after index procedure	3.5 (23)	1.9 (113)	0.08
TVMI between 1 month and 12 months after index procedure	0.9 (6)	0.2 (1)	0.13
Overall angiographic complications at the end of procedure for TVMI within 1 month	3.1 (20)	1.7 (10)	0.14
Side-branch occlusion	2.3 (15)	1.4 (8)	0.29
Coronary dissection	1.1 (7)	0.3 (2)	0.18
Side branch occlusion + coronary dissection	0.3 (2)	0 (0)	0.50
Not relating to device caused angiographic complications for TVMI within 1 month	0.3 (2)	0.3 (2)	1.0
Coronary dissection due to balloon dilation			

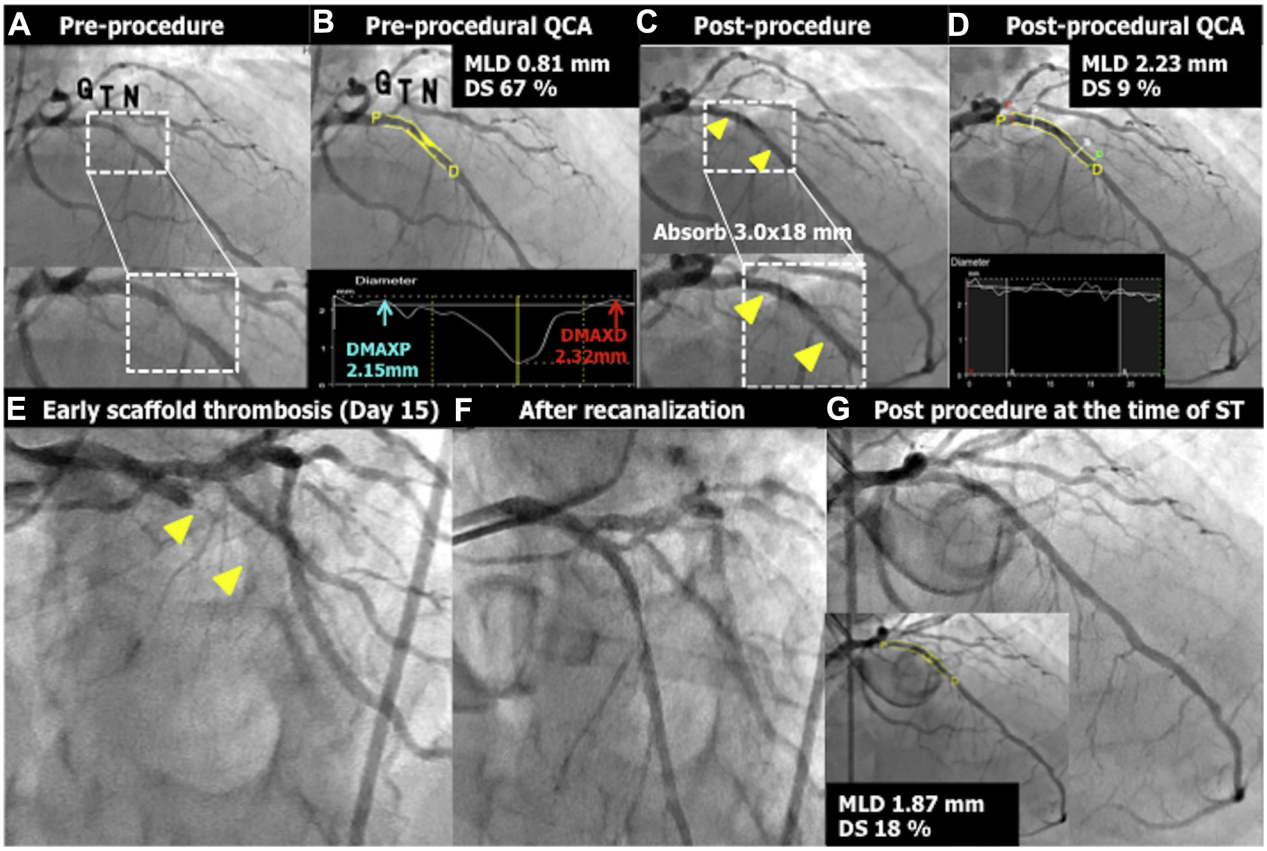
Values are % (n).

Abbreviations as in Table 2.

Retrospective subanalysis (8) of the ABSORB Cohort B study demonstrated that after implantation of a 3.0 × 18-mm device, patients with a Dmax ranging between 2.5 and 3.3 mm had better acute OCT outcomes as compared with patients with a Dmax out of range. The implantation of a "small" Absorb scaffold in a relatively large vessel can cause incomplete strut apposition at the edge and may be associated with scaffold disruption (9) when aggressive postdilation with a larger balloon is attempted to correct such malapposition (Figure 6A). Conversely, implantation of a "large" Absorb scaffold in a relatively small vessel can cause vessel injury or underexpansion of the scaffold (Figure 6B).

CLINICAL OUTCOMES WITH RESPECT TO Dmax. The present study clearly demonstrates that implanting Absorb scaffold(s) in a vessel with both proximal and distal Dmax smaller than the device

FIGURE 5 **A Case Example of a Definite Early Thrombosis of Absorb Scaffold Implanted in the Mid-LAD**



The patient received a 3.0-mm device in a too-small vessel (proximal and distal Dmax 2.15 mm and 2.32 mm, respectively **[A and B]**). After Absorb scaffold implantation **(C and D, arrowheads)**, QCA showed an excellent result with a residual DS of 9%. Fifteen days after the procedure, the patient presented with a STEMI due to early scaffold thrombosis **(E)** that was treated with a manual aspiration only **(F and G)**. DS = diameter stenosis; LAD = left anterior descending coronary artery; ST = scaffold thrombosis; STEMI = ST-segment elevation myocardial infarction; other abbreviations as in Figure 1.

nominal size is associated with a higher risk of ID-MACE (6.6% vs. 3.3%; $p < 0.01$). The difference in 1-year MACE was observed in the scaffold oversize group and was mainly driven by a higher MI rate (4.5% vs. 2.1%; $p < 0.01$). Scaffold expansion below nominal diameters can lead to a denser polymer surface pattern and a higher polymer-to-artery ratio (Online Figure 3). Furthermore, the expanding radial force may be suboptimal in these underdeployed configurations; presumably, these unfavorable final expansion diameters might cause micro thrombus formation at the strut level and side-branch occlusion. However, no statistically significant difference in the incidence of overall angiographic complications could be documented at the end of the procedure for the patients who sustained MI within 1 month (scaffold oversize group: 3.1% vs. scaffold nonoversize group: 1.7%; $p = 0.14$) (Table 3).

With multivariable logistic regression analysis, the independent determinants of 1-year MACE were: implantation of an Absorb scaffold(s) in a vessel with both proximal and distal Dmax smaller than device nominal size (OR: 2.13, 95% CI: 1.22 to 3.70; $p < 0.01$) and overlapping scaffolds (OR: 2.10, 95% CI: 1.17 to 3.80; $p = 0.01$) (Table 4). Of note, in a juvenile porcine model, overlapping Absorb scaffolds showed delayed healing on histology and with OCT assessment and slower tissue coverage than nonoverlapping scaffolds. Indeed, the neoendothelial coverage of the overlapping segments was 80.1% and 99.5% at 28 and 90 days after implantation, respectively; accordingly, coverage in humans may need up to 18 months to be completed (16). Among the 62 patients with MACE,

TABLE 4 Predictors of MACE After Implantation of the Absorb Scaffold(s)

	Univariate Logistic Regression		Multivariate Logistic Regression	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Age, yrs	1.01 (0.98–1.03)	0.64	–	–
Male	0.83 (0.47–1.46)	0.52	–	–
Current smoker	0.80 (0.42–1.53)	0.51	–	–
Hypertension requiring treatment	1.00 (0.90–1.10)	0.96	–	–
Dyslipidemia requiring treatment	1.54 (0.84–2.83)	0.16	–	–
Any diabetes mellitus	0.78 (0.42–1.46)	0.44	–	–
Unstable angina	0.69 (0.35–1.34)	0.27	–	–
Prior myocardial infarction	1.01 (0.99–1.04)	0.20	–	–
Pre-procedural diameter stenosis, %	0.99 (0.97–1.02)	0.55	–	–
Pre-procedural MLD, mm	0.76 (0.33–1.72)	0.51	–	–
Obstruction length, mm	0.99 (0.94–1.04)	0.64	–	–
Smallest Dmax (proximal and distal)	0.51 (0.22–1.14)	0.10	–	–
Angulation ≥45°	0.64 (0.09–4.81)	0.67	–	–
Moderate/severe calcification	0.65 (0.28–1.54)	0.33	–	–
Pre-procedural visible thrombus	0.94 (0.12–7.13)	0.95	–	–
Bifurcation lesion	CS	CS	–	–
Type B2/C lesion	1.02 (0.61–1.71)	0.93	–	–
Left anterior descending artery	0.73 (0.43–1.23)	0.24	–	–
Nominal scaffold size/post-procedural MLD	3.11 (0.73–13.16)	0.12	–	–
Treatment with overlapping devices	2.08 (1.15–3.75)	0.02	2.10 (1.17–3.80)	0.01
2.5-mm device implanted	0.69 (0.27–1.75)	0.44	–	–
Implanting Absorb scaffold(s) in a vessel with both proximal and distal Dmax smaller than nominal size of the device	2.11 (1.21–3.66)	0.01	2.13 (1.22–3.70)	<0.01

CS = complete separation; ITT = intention to treat; MLD = minimal lumen diameter; other abbreviations as in Table 2.

MI occurred in 14 (22.6%) patients who were treated with overlapping scaffolds and were mainly PMI (12 [19.4%]). Thus, overlapping of scaffolds might be a contributing factor of MACE.

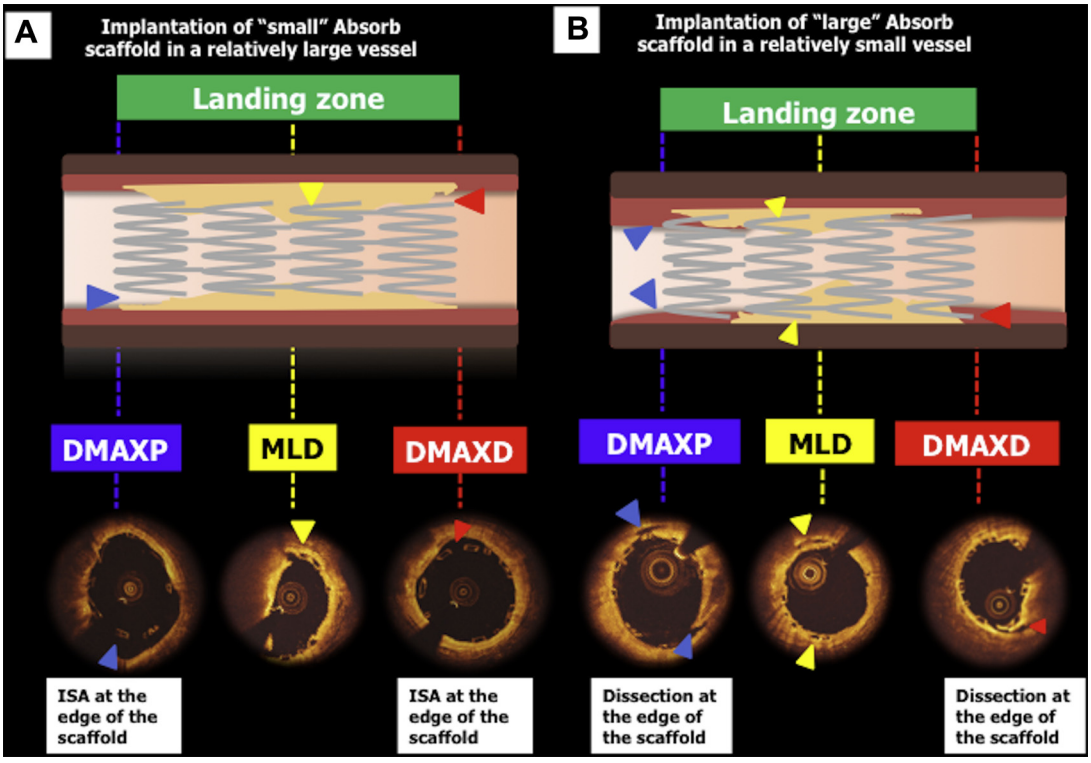
PRACTICAL IMPLICATIONS OF THE SELECTION OF APPROPRIATELY SIZED ABSORB SCAFFOLDS. Previously, we have focused mainly on the upper limit of 0.5 mm Dmax due to the well-known issues of device malapposition and disruption in case of over dilation. However, scaffold underexpansion due to the deployment of a scaffold in a vessel with a smaller size, may be associated with a higher post-procedural MI rate due to several different mechanisms. The oversized scaffold could create vessel dissection or microperforation in a small target vessel. Alternatively, the underexpansion of the scaffold may lead to a denser polymer surface pattern and a larger strut footprint to vessel surface area causing side branch occlusion or microthrombus formation.

In the present study, the size selection of Absorb scaffolds with the cutoff value of 0.5-mm Dmax has been shown to be clinically relevant. As presented in the Results and Online Appendix, more events were observed when the mismatch between the device and the vessel size was beyond 0.4 mm. It could therefore be recommended that the device-vessel mismatch regarding Dmax should be within 0.4 mm.

The current analysis showed that the device-vessel mismatch regarding the pre-procedural angiography has a clinical impact. There were no differences in MACE in the population with a post-procedure diameter stenosis ≥10% and <10% (MACE: 5.3% vs. 4.1%; p = 0.46) or in patients with a diameter stenosis ≥20% and <20% (MACE: 5.14% vs. 4.69%; p = 0.77). Therefore, the observed relationship between device-vessel mismatch and clinical outcomes seems to specifically relate to pre-procedural angiographic measurement. It is still unclear how far the pre-procedural device-vessel mismatch could be corrected by post-dilation with high-pressure or low-pressure balloons. Currently, operators with a large experience of BRS implantation are intuitively promoting a strategy of a high-pressure post-dilation with a noncompliant balloon size 0.25 or 0.5 mm larger than the nominal size of the device. A randomized trial on post-dilation strategy (systematic vs. nonsystematic) will be able to clarify what the optimal implantation technique for this polymeric coronary device is.

It has been shown that QCA underestimates coronary lumen diameter, whereas OCT provides correct assessment of lumen dimension (17). Mattesini et al. (18,19) reported that when OCT is used to guide and optimize Absorb scaffold implantation, post-implantation area stenosis, minimal lumen area, and eccentricity index were similar to those observed after deployment of second-generation metallic drug-eluting stents. The different approach for lesion preparation and routine use of OCT guidance during Absorb scaffold implantation might have contributed to these results. In addition, recent studies demonstrated with multivariable analysis that peristent dissections shown by OCT were independent predictors of PMI (OR: 5.3, 95% CI: 1.2 to 24.3), raising concerns about the relationship between these minor vessel injuries and a potential higher risk of early TVMI (20). Taking into account the weakness of QCA for accurately measuring vessel lumen dimension and its inability to assess incomplete scaffold apposition and/or acute scaffold disruption, coregistration (21) of OCT imaging and x-ray angiography may be useful for optimizing the percutaneous treatment of coronary artery disease with bioresorbable vascular scaffolds. In future studies, a clinical scientific question would be whether the pre-procedural usage of intravascular imaging could further improve clinical outcomes.

FIGURE 6 The Potential Consequences of a Device-Vessel Mismatch Implantation



Implantation of a too "small" Absorb scaffold in a relatively large vessel can cause incomplete apposition of the device edges **(A, top panel, blue and red arrowheads)**. Incomplete scaffold apposition **(blue and red arrow heads)** and scaffold under-expansion **(yellow arrowhead)** are visible in the OCT images **(A, bottom panel)**. Implantation of a too "large" Absorb scaffold in a relatively small vessel can cause vessel injury **(B, top panel, blue and red arrowheads)**. Edge dissections **(blue and red arrowheads)** are visible in the OCT images **(B, bottom panel)**. ISA = incomplete scaffold apposition; OCT = optical coherence tomography; other abbreviations as in Figure 1.

STUDY LIMITATIONS. The current study does not provide mechanistic data to support the occurrence of clinical adverse events caused by sizing mismatch due to a lack of routine intravascular imaging (e.g., intravascular ultrasound, OCT, etc.). Further investigation using intravascular imaging is needed to establish the relationship between acute mechanistic complications (such as underexpansion, dissection, and malapposition, and so on) and late adverse events.

CONCLUSIONS

Selection of an appropriate scaffold size according to the vessel Dmax showed a trend toward less frequent ID-TLR, whereas implantation of an oversized Absorb scaffold in a relatively small vessel may be associated with a higher risk of MACE at 1 year. The current results need to be confirmed in the large-scale randomized trials that are on-going, and the mechanistic etiologies should be further elucidated in imaging studies.

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PERSPECTIVES

WHAT IS KNOWN? QCA-Dmax–guided scaffold size selection has been proposed to optimize the scaffold implantation procedure. However, the relationship between clinical outcomes and QCA-Dmax is unknown.

WHAT IS NEW? The device-vessel size mismatch has an impact on clinical event after implantation of Absorb scaffold.

WHAT IS NEXT? The current results should be confirmed in large-scale randomized trials, and the mechanistic etiologies should be further elucidated in studies using intravascular imaging.

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KEY WORDS bioresorbable scaffold, major adverse cardiac event(s), maximal lumen diameter

APPENDIX For supplemental figures and tables, please see the online version of this article.