

BRS Failure Analysis: Lessons from Serial Imaging Studies

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Meta-analysis of long-term outcomes after the ABSORB implantation

Collet et al. ABSORB II 1,730 1,015 v: $1,750$ ABSORB ABSORB ABSOR 2Y 2Y 0.3% vs. 6.6% 0.90-2.42 0.6% vs. 1.6% 0.90-2.42 OR 1.89 0.81-6.19 OR 2.95 0.115-3.13 OR 2.95 0.137-6.26 OR 3.04 0.120-7.68 Ha ABSORB II 2Y OR 1.48 0.90-2.42 OR 2.25 0.81-6.19 OR 1.89 0.15-3.13 OR 2.95 0.137-6.26 OR 3.04 0.120-7.68 Ha ABSORB II 2Y ABSORB II 2Y ABSORB II Y ABSORB II 2Y ABSORB II 2Y ABSORB II Y ABSORB II Y ABSORB II 2Y ABSORB II 2Y ABSORB II Y ABSORB II Y ABSORB II 2Y ABSORB II Y ABSORB II Y ABSORB II Y ABSORB III 3Y X X X X X X X X ABSORB III 3Y X X X X X X X X X X X X X X X X<	Study	Number of included patients	f Included study	follow-up year	TLF rate (BVS vs EES) OR (95%CI)	TV-MI (BVS vs EES) OR (95%CI)	ID-TLR rate (BVS vs EES) OR (95%CI)	Definite/ probable ST rate (BVS vs EES) OR (95%CI)	Very late ST rate (BVS vs EES) OR (95%CI)
Collet 1,730 ABSORB 2Y 9.3% vs. 6.6% 4.5% vs. 1.6% 5.6% vs. 3.0% 2.4% vs. 0.9% 1.4% vs. 0.5% et al. ¹ 1,730 ABSORB 2Y OR 1.48 OR 2.25 OR 1.89 OR 2.95 OR 3.04 TROFI II 2Y IROFI II 3Y IROFI II 3Y IROFI II			ABSORB II	3Y					
connect et al. ¹ (1,015 vs. 715) ABSORB (CHINA 2Y OR 1.48 (0.90-2.42) OR 2.25 (0.81-6.19) OR 1.89 (1.15-3.13) OR 2.95 (1.37-6.26) OR 3.04 (1.20-7.68) Ha et al. ³ TROFI II EVERBIO II 2Y ABSORB II ABSORB 3Y ABSORB JAPAN ABSORB 2Y OR 1.31 (0.93-1.83) OR 2.59 (0.81-6.19) OR 1.70 (1.02-2.83) OR 2.35 (1.14-4.86) Not reported Ha et al. ³ 2,582 (1,407 vs. 1,095) ABSORB BSORB EXAMINATIO 2Y OR 1.31 (0.93-1.83) OR 2.59 (1.17-5.70) OR 1.70 (1.02-2.83) OR 2.35 (1.14-4.86) Not reported Ha et al. ³ ABSORB 1,095) 3Y ABSORB II ABSORB 2Y OR 1.31 (0.93-1.83) OR 2.59 (1.17-5.70) OR 1.70 (1.02-2.83) OR 2.35 (1.14-4.86) Not reported Ha et al. ³ ABSORB II ABSORB 3Y ABSORB II ABSORB 2Y ABSORB 2Y 2Y 2Y 2Y 2Y </td <th>Collet</th> <td>1,730</td> <td>absorb Japan</td> <td>2Y</td> <td>9.3% vs. 6.6%</td> <td>4.5% vs. 1.6%</td> <td>5.6% vs. 3.0%</td> <td>2.4% vs. 0.9%</td> <td>1.4% vs. 0.5%</td>	Collet	1,730	absorb Japan	2Y	9.3% vs. 6.6%	4.5% vs. 1.6%	5.6% vs. 3.0%	2.4% vs. 0.9%	1.4% vs. 0.5%
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ABSORB 2Y 0.69(up 7.29(ABSORB II	3Y					
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no (3,261 vs. ABSORB CHINA 2Y OR 1.32 OR: 1.62 OR 1.40 OR 3.15 OR 3.96	no ot al ²	(3,261 vs. 2,322)	ABSORB CHINA	2Y	OR 1.32	OR: 1.62	OR 1.40	OR 3.15	OR 3.96
AIDA 2Y (1.1-1.59) (1.24 to 2.12) (1.10-1.79) (1.87-5.30) (1.47-10.66)	et al. ²	,,	AIDA	2Y	(1.1-1.59)	(1.24 to 2.12)	(1.10-1.79)	(1.87-5.30)	(1.47-10.66)
TROFI II 2Y			TROFI II	2Y					
EVERBIO II 2Y			EVERBIO II	2Y					

1; EHJ. 2017, 2; JACC 2017, 3; JACC Cardiovasc Interv. 2017.



BRS Failure Analysis: Lessons from Serial Imaging Studies

- 1.What are the imaging findings at the time of acute, subacute and late/very late Scaffold Thrombosis?
- 2.What are post-procedural imaging findings correlating to very late scaffold thrombosis?
- 3.What is the relationship of scaffold discontinuities and very late scaffold thrombosis?



Sotomi et al. El 2016

Peri-strut low intensity area

Uncovered struts

Neoatherosclerosis

Possible mechanical causes of scaffold thrombosis: insights from case reports with intracoronary imaging



Yohel Sotemi¹, MD; Pannipa Suwannasom^{1,1,3}, MD; Patrick W. Serruys¹⁴, MD, PhD; Yoshinoba Onuma³, MD, PhD

Systematic review

Imaging findings in ScT cases

• Early ScT (N=17) malapposition (24%), incomplete lesion coverage (18%), and underdeployment (12%)

• Late/very late ScT (N=26) malapposition (35%), late discontinuity (31%) and peri-strut low-intensity area (19%)



Early scaffold thrombosis



Late/very late scaffold thrombosis





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Scaffold or stent thrombosis in ABSORB II trial

	Absorb 335 patients	Xience 166 patients	p value
Definite	2.5% (8)	0.0% (0)	0.06
Acute (0–1 day)	0.3% (1)	0.0% (0)	1.0
Sub-acute (2–30 days)	0.3% (1)	0.0% (0)	1.0
Late (31–365 days)	0.0% (0)	0.0% (0)	1.0
Very late (>365 days)	1.8% (6)	0.0% (0)	0.19

2:1 randomization

- The ABSORB II trial was plagued by the unexpected occurrence of very late scaffold thromboses, although the observation did not reach statistical significance when compared to the non-occurrence of VLST in the Xience arm.
- It is hypothesized that these late and very late events (up to 3 years) are related to the acute suboptimal implantation results such as under-expansion and malapposition.
- The objective of the current study is to investigate the possible relationship of baseline demographics, post-procedural angiographic and ultrasound imaging results with the occurrence of definite very late scaffold thromboses in the Absorb II trial, in order to unravel potential mechanism of very late complications.

Serruys et al. 2017 CRT

Prospective analysis by core laboratory blind for events

Impacts of pre-procedure, device sizing and post-dilatation related parameters on VLScT

QCA parameter

- Reference vessel diameter pre-device implantation
- Device sizing with reference to pre-reference vessel diameter

IVUS parameter

- Reference lumen diameter pre-device implantation
- Device sizing with reference to pre-reference lumen diameter

Procedure

- Final balloon (nominal)/device ratio
- Maximal final-dilatation balloon pressure

Serruys et al. 2017 CRT

Impacts of post-procedural parameters on VLScT

QCA parameter

- Percent diameter stenosis
- Minimum lumen diameter
- Lesion coverage ratio

IVUS parameter

- Minimum lumen diameter
- Expansion index
- Minimum eccentricity index
- Asymmetry index
- Deployment index
- Maximal ISA distance

QCA parameter

- Percent diameter stenosis
- Minimum lumen diameter
- Lesion coverage ratio

IVUS parameter

- Minimum lumen diameter
- Expansion index
- Minimum eccentricity index
- Asymmetry index
- Deployment index
- Maximal ISA distance

(%) Absorb n=364 10-* VLScT (n=6) Percentage 5 (%) Percentage 5 10-Xience n=182 10 20 30 50 40 (%) % Diameter stenosis by QCA

% Diameter stenosis

QCA

QCA parameter

- Percent diameter stenosis
- Minimum lumen diameter
- Lesion coverage ratio

IVUS parameter

- Minimum lumen diameter
- Expansion index
- Minimum eccentricity index
- Asymmetry index
- Deployment index
- Maximal ISA distance



Lesion coverage ratio = Stent length / pre-lesion length



QCA parameter

- Percent diameter stenosis
- Minimum lumen diameter
- Lesion coverage ratio

IVUS parameter

- Minimum lumen diameter
- Expansion index
- Minimum eccentricity index
- Asymmetry index
- Deployment index
- Maximal ISA distance

Expansion index

The higher value indicates more expanded device





Serruys et al. 2017 CRT

QCA parameter

- Percent diameter stenosis
- Minimum lumen diameter
- Lesion coverage ratio

IVUS parameter

- Minimum lumen diameter
- Expansion index
- Minimum eccentricity index ٠
- Asymmetry index ٠
- Deployment index
- Maximal ISA distance



Predictors for VLScT: Univariate Cox regression analysis

Variable	Odds ratio [95% confidence interval]	p value
Procedure		
Post-dilatation performed	0.55 [0.11-2.78]	0.471
Post-dilatation maximal pressure (atm)	0.76 [0.51-1.13]	0.176
QCA		
In-device % diameter stenosis (%)	1.07 [0.96-1.19]	0.218
In-device minimum lumen diameter (mm)	2.58 [0.25-26.08]	0.422
Lesion coverage ratio per 0.1 increase	0.74 [0.56-0.98]	0.032
IVUS		
Minimum lumen diameter (mm)	1.80 [0.18-17.74]	0.613
Asymmetry index per 0.1 increase	0.34 [0.10-1.18]	0.088
Expansion index per 0.1 increase	0.58 [0.32-1.04]	0.066
Minimum eccentricity index per 0.1 increase	2.29 [0.63-8.35]	0.208
Deployment index per 0.1 increase	1.78 [0.75-4.22]	0.188
Expansion index <0.6	6.93 [1.24-38.82]	0.028

Serruys et al. 2017 CRT



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Molecular weight, Mechanical support and Mass loss



Possible mechanical causes of scaffold thrombosis: insights from case reports with intracoronary imaging



Yohel Sotemi¹, MD; Pannipa Suwannasom^{1,1,3}, MD; Patrick W. Serruys¹⁴, MD, PhD; Yoshinoba Onuma³, MD, PhD

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• Early ScT (N=17) malapposition (24%), incomplete lesion coverage (18%), and underdeployment (12%)

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Early scaffold thrombosis



Late/very late scaffold thrombosis



3 criteria to judge acute disruption/late discontinuities on OCT

	Time of OCT observation			
	Post procedure	Late		
	 Stacked struts 			
Acute Scaffold disruption	•Overhung struts	Persistent		
	 Isolated intra- luminal strut(s) 			
Late Scaffold discontinuities	No disruption	 Stacked/ overhung / isolated or intraluminal strut (s) 		



Late discontinuities observed in porcine coronary artery





Serial changes of strut distribution



ABSORB Cohort B2

BRS textbook

S.	Baseline	12 months	36 months
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In serial OCT observation up to 36 months, late discontinuities were observed in 43%, without clinical events

Onuma et al. JACC int 2014,

Case 3: Late Discontinuities observed at 2-year planned FUP OCT (Uncovered and malapposed), Absorb Japan Onuma et al. EuroIntervention. 2016



Reference diameter 1.82 mm Minimum lumen diameter 0.67 mm %DS 67%

Pre-dilatation 2.5mm x 14 atm >>> BVS 2.5 x 28 mm >>>Post-dilatation 2.75 x 22 atm Case 3: Late Discontinuities observed at 2-year planned FUP OCT (Uncovered and malapposed), Absorb Japan Onuma et al. EuroIntervention. 2016 Neointimal coverage

>300um

200-300 um100-200 um

0-100 umUncovered

Malapposed

Late discontinuity No1

WL: 178 WW: 127

Covered by neointima

Late discontinuity No2

WL: 178 WW: 127

Protruded into the lumen



#4. VLST case 1 (Day 494)Onuma et al. Eurointervention 2016Risk factors: 79 yo M, HTN, HL, former smoker, DM II

Pre-PCI

Target lesion

pLAD with moderate calcification **QCA analysis** Lesion length 14 mm Proximal reference diameter 3.77 mm Distal reference diameter 2.76 mm Proximal Dmax 3.92mm/Distal Dmax 2.89mm

Post-PCI

Pre-dilatation >>> BVS 3.5 x 28 mm >>>Post-dilatation 3.5 x 18 atm

QCA analysis Minimum lumen diameter 2.56 mm

13months follow-up CAG



QCA analysis minimum lumen diameter 2.52 mm

#4. VLST (day 494) (TVQMI)

Post thrombectomy



Imaging findings associated with Late/very late scaffold thrombosis reported in literature





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- Malapposition, incomplete plaque coverage, overlap and underexpansion are frequently observed in intracoronary imaging at the time of early scaffold thrombosis, whereas malapposition, late discontinuity and peristrut low-intensity were reported by imaging at the time of late/very late scaffold thrombosis.
- Despite the small number of patients and events, Absorb II imaging analysis suggested a correlation between the **under-expansion** and the occurrence of VLScT after implantation of Absorb scaffold.
- Late discontinuity is in general a benign change during the bioresorption process and does not cause any problems if struts are well covered. However, in case struts are not covered by neointima and late discontinuity lets protrude part of the struts into the lumen, late discontinuity could be a malignant potential cause of ScT. Enhancement of neointimal coverage would be a key to prevent ScT associated with late discontinuity. Further research is needed to investigate what triggers VLST.