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ORIGINAL ARTICLE

Neointimal coverage and late apposition of everolimus-eluting bioresorbable scaffolds implanted in the acute phase of myocardial infarction: OCT data from the PRAGUE-19 study

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Abstract Incomplete stent apposition and uncovered struts are associated with a higher risk of stent thrombosis. No data exist on the process of neointimal coverage and late apposition status of the bioresorbable vascular scaffold (BVS) when implanted in the highly thrombogenic setting of ST-segment elevation acute myocardial infarction (STEMI). The aim of this study was to assess the serial changes in strut apposition and early neointimal coverage of the BVS using optical coherence tomography (OCT) in selected patients enrolled in the PRAGUE-19 study. Intracoronary OCT was performed in 50 patients at the end of primary percutaneous coronary intervention for acute STEMI. Repeated OCT of the implanted BVS was performed in 10 patients. Scaffold area, scaffold mean diameter and incomplete strut apposition (ISA) were compared between baseline and control OCT. Furthermore, strut neointimal coverage was assessed during the control OCT. Mean scaffold area and diameter did not change between the baseline and control OCT (8.59 vs. 9.06 mm^2; $p = 0.129$ and 3.31 vs. 3.37 mm; $p = 0.202$, respectively). Differences were observed in ISA between the baseline and control OCT (0.63 vs. 1.47 %; $p < 0.05$). We observed 83.1 % covered struts in eight patients in whom the control OCT was performed 4–6 weeks after BVS implantation, and 100 % covered struts in two patients 6 months after BVS implantation. Persistent strut apposition and early neointimal coverage were observed after biodegradable vascular scaffold implantation in patients with acute ST-segment elevation myocardial infarction.

Keywords Biodegradable vascular scaffold · Neointimal coverage · Late apposition · Acute myocardial infarction

Abbreviation

PCI	Percutaneous coronary intervention
BVS	Bioresorbable vascular scaffold
OCT	Optical coherence tomography
STEMI	ST-segment elevation myocardial infarction
ISA	Incomplete strut apposition

Introduction

The number of percutaneous coronary interventions (PCI) using bioresorbable vascular scaffolds (BVS) has increased since the device became commercially available in several countries. The ABSORB Cohort B and ABSORB EXTEND trials showed good mid-term efficacy and safety after implantation of the ABSORB second-generation device (BVS 1.1) in patients with stable *de novo* coronary artery lesions [1, 2]. Good procedural and late apposition of the BVS as well as almost complete stent neointimal coverage after 6 months were confirmed in this group of patients using optical coherence tomography (OCT) [1, 3–5].

Recently, several prospective small studies showed that BVS can be used safely and effectively in patients with acute coronary syndrome, including those presenting with ST-segment elevation myocardial infarction (STEMI) [6–10]. Even though OCT has yielded very good procedural results after BVS implantation [7, 9], no data on BVS late apposition and neointimal coverage in a clinical setting

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exist, and such information is critical. The correct use of the appropriate stent size in STEMI patients is challenging due to vasoconstriction; residual thrombus treated using BVS may dissolve over time, and this can lead to acquired incomplete BVS apposition, slower neointimal coverage and augmented risk of BVS thrombosis and further adverse clinical outcome [11].

Therefore, the purpose of this study was to evaluate by OCT late apposition and neointimal coverage of implanted BVS during primary PCI in patients with STEMI.

Methodology

The PRAGUE-19 is an academic prospective study to evaluate the effect of BVS 1.1 Absorb (Abbott Vascular, Santa Clara, CA, USA) as a default strategy during primary PCI in patients with STEMI. The inclusion and exclusion criteria used in this study have been published previously [9]. Intracoronary OCT imaging was performed at the end of the primary PCI and achieved optimal angiographic results in patients without haemodynamic deterioration, ventricular arrhythmias, or a large contrast load during the procedure. The methodology for the OCT measurements was described previously [9].

This study included selected patients who underwent staged PCI of a non-infarct vessel or had a clinical indication for repeated coronary angiography during follow-up, along with available baseline OCT measurements. The protocol of the study was approved by the local ethical committee and written informed consent was obtained from all study patients. During the repeated procedure, OCT of the infarcted vessel with implanted BVS was performed using the frequency domain C7 system with a Dragonfly catheter (St. Jude Medical, St. Paul, MN, USA), a pullback speed of 20 mm/second, and an image acquisition of 100 frames/second. Cross-sections were analysed at each 1-mm interval within the stented segment and at 5 mm proximal and distal positions. Scaffold area, scaffold mean diameter and incomplete strut apposition (ISA) and ISA area were compared between the baseline and control OCT. With clear landmarks in the longitudinal OCT images, all cross-section at baseline were matched with the corresponding image at follow-up. Furthermore, strut neointimal coverage was assessed during the control OCT. Strut discontinuity was also assessed at baseline and control OCT and was defined as the presence of two overhanging struts or an isolated strut in the centre of the vessel with no obvious connection to other struts. At baseline and follow-up, struts with incomplete apposition were defined as struts in which the abluminal surfaces were separated from the vessel wall by flush and masses attached to the vessel wall. Missing neointimal coverage at follow-up was identified as struts forming preserved right angles without signs of neointimal tissue [4]. Strut apposition and neointimal coverage were determined according to the consensus reached between the two investigators who evaluated the OCT measurements.

Standard descriptive statistics were applied in the analyses: absolute and relative frequencies for categorical variables and means and standard deviations for the continuous variables. Statistical significance of differences between groups of patients was computed using Fisher's exact test for two-category variables, maximum-likelihood test for variables with more than two categories, and independent *t* test for continuous variables. Independent observation (analysis of data at the cross-section level after matching baseline and control OCT) was used for comparison of ISA. A paired *t* test was used to evaluate the statistical significance of differences between measurements of vessel and scaffold area and diameter. The level of statistical significance was set at $p < 0.05$.

Results

Study group characteristics

Eighty-two patients were enrolled in the PRAGUE-19 study from December 2012 to May 2014; OCT was performed in 50 patients at the end of the primary PCI. Planned staged PCI of the non-infarcted coronary artery was performed in eight patients, with a mean delay of 37 days after the primary PCI. Coronary angiography was indicated due to clinical symptoms of unstable angina pectoris after 6 months in two patients, both of whom underwent PCI of the non-infarcted coronary artery. Thus, ten patients underwent controlled OCT of the previously implanted BVS during the repeated procedure. The clinical characteristics of these 10 patients are listed in Table 1. After the primary PCI, no major clinical events (stent thrombosis, myocardial infarction, stroke, major bleeding) occurred in these 10 patients during the follow-up. The procedural aspects of the primary PCI are listed in Table 2.

Table 1 Patient characteristics

Age, years (SD)	61 (8)
Men, *n* (%)	8 (80)
Diabetes mellitus, *n* (%)	1 (10)
Hypertension, *n* (%)	4 (40)
History of PCI or CABG, *n* (%)	0 (0)
History of MI or stroke, *n* (%)	0 (0)
Active smoking, *n* (%)	7 (70)
KILIP I during pPCI, *n* (%)	10 (100)
Ejection fraction at discharge, % (SD)	52 (10)

Table 2 Procedural aspects of the primary PCI of patients with control OCT at follow-up

Infarct related artery	
LAD, *n* (%)	3 (30)
LCx, *n* (%)	1 (10)
RCA, *n* (%)	6 (60)
Predilatation, *n* (%)	8 (80)
Thromboaspiration, *n* (%)	4 (40)
Postdilatation, *n* (%)	2 (20)
Glycoprotein IIb/IIIa inhibitors, *n* (%)	5 (50)
Number of BVS per patient, mean (SD)	1.4 (0.7)
Length of implanted BVS per patient, mean (SD)	29 (15) mm
Range of the length of implanted BVS	18–64 mm
Size of implanted BVS, mean (SD)	3.25 (0.42) mm
Edge dissection seen on OCT after pPCI, *n* (%)	5 (50)
Use of $P2Y_{12}$ receptor blockers	
Prasugrel, *n* (%)	7 (70)
Ticagrelor, *n* (%)	3 (30)

Baseline and controlled OCT comparisons

For the baseline and controlled OCT measurements, 229 and 227 frames with 2242 and 2208 struts of implanted BVS were evaluated, respectively. Table 3 lists the comparisons between the baseline and controlled OCT measurements in terms of vessel reference and scaffold dimensions and the number of struts with incomplete apposition. At baseline ISA was observed in 0.62 % of struts. In eight patients with controlled OCT performed 4–6 weeks following primary PCI, ISA was detected in 32 of 1741 (1.84 %) struts. In two patients who underwent controlled OCT 6 months after the primary PCI, ISA was observed in 3 of 467 struts (0.64 %). By matching cross-sections from baseline and control OCT, 28.6 % of ISA at follow-up persisted from baseline and late-acquired ISA were detected in 62.9 % (8.5 % ISA were unmatchable).

Table 3 Comparison between the baseline and controlled OCT measurements of segments with implanted BVS

	Baseline OCT	Controlled OCT	*p* value
Proximal mean reference area	8.98 ± 1.71 mm^2	9.24 ± 2.05 mm^2	0.301
Distal mean reference area	6.7 ± 1.8 mm^2	7.55 ± 1.4 mm^2	0.027
Proximal mean reference diameter	3.36 ± 0.30 mm	3.39 ± 0.59	0.380
Distal mean reference diameter	2.87 ± 0.33 mm	3.11 ± 0.34 mm	0.025
Scaffold mean area	8.53 ± 1.29 mm^2	8.98 ± 1.64 mm^2	0.135
Scaffold mean diameter	3.29 ± 0.28 mm	3.35 ± 0.31 mm	0.229
Thrombus detected/% of patients	80 %	20 %	0.007
Struts with incomplete apposition	0.62 %	1.59 %	0.003
ISA area	0.10 ± 0.19 mm^2	0.15 ± 0.21 mm^2	0.116

In five patients, the BVS edge dissection was present on the OCT images at the end of the primary PCI when the angiographic result was optimal. These dissections were not seen during the controlled OCT. Thrombi at the site of the implanted BVS were detected in eight out of 10 patients and in 19.8 % of frames in the baseline OCT images, but only in two patients and 4 % of frames in the controlled OCT images during the follow-up ($p < 0.001$). At baseline, no BVS discontinuity was detected, but was observed in two patients (two frames in both cases) during the follow-up (Fig. 1). The proximal reference diameter measured by OCT was larger by 0.27 (± 0.49) mm than proximal diameter measured by QCA ($p < 0.05$) during the baseline evaluation as well as during the follow-up examination (0.25 ± 0.38 mm, $p < 0.05$), respectively.

Assessment of neointimal coverage

In eight patients with controlled OCT performed after a mean delay of 37 days following primary PCI, neointimal coverage was detected in 1446 of 1741 (83.1 %) struts (Fig. 2). Of 467 evaluated struts, 100 % were covered in two patients who underwent controlled OCT 6 months after the primary PCI (Fig. 3). Of 295 non-covered struts, 269 (91.2 %) were apposed to the vessel wall, 21 (7.1 %) had ISA and five (1.7 %) were located over the side branch. Non-covered struts were observed in 21 of 35 (60 %) struts with ISA, 5 of 11 (45 %) were located over the side branch and 269 of 1749 (15 %) were apposed struts ($p < 0.001$).

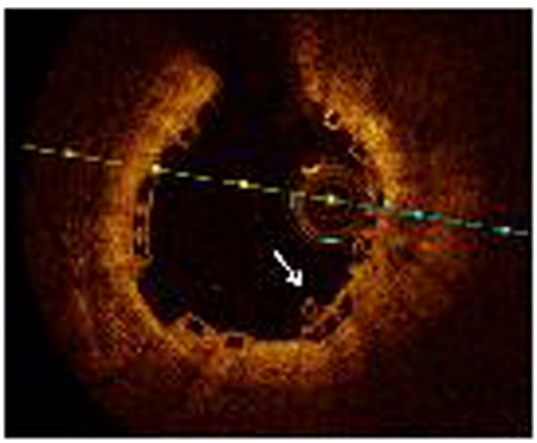

Fig. 1 BVS discontinuity. Discontinuity of the BVS seen as two overhanging struts (flash) during controlled OCT in patient 31 days after PCI

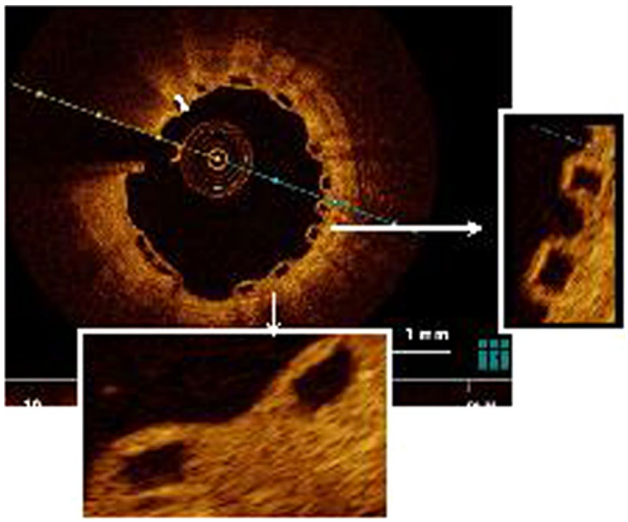

Fig. 2 Early BVS neointimal coverage. OCT image 1 month after BVS implantation. The *lower* portion of the image shows magnification of two covered struts, and the *right* side shows magnification of two struts without coverage

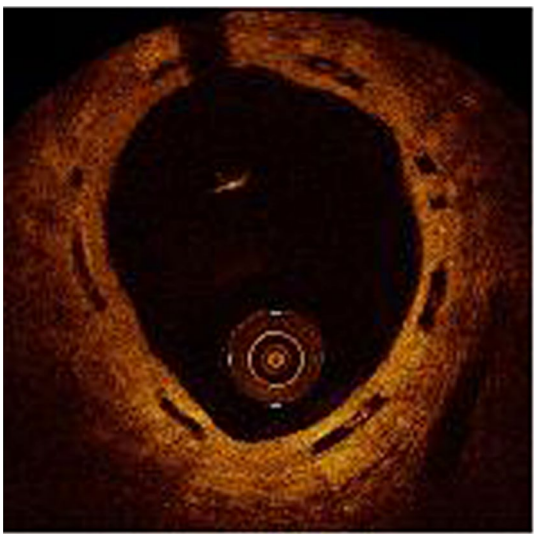

Fig. 3 BVS neointimal coverage at 6 months. Complete struts coverage seen during the OCT performed 6 months after implantation of the BVS

Discussion

In our study, OCT highlighted the ongoing effects of BVS implanted during primary PCI in patients with STEMI, with early neointimal coverage occurring after approximately 1 month.

Several studies on OCT measurement have reported results from different follow-up periods after BVS implantation [1, 3, 4]. Nevertheless, these studies involved patients with BVS implanted in the context of stable coronary artery disease. The highly thrombotic condition with possible vasoconstriction in STEMI patients presents a much more challenging situation, and to date there exist no data from a controlled OCT.

In terms of BVS apposition, significantly more ISA was detected during the follow-up compared with the acute phase after BVS implantation. This was especially done by acquired ISA in the middle portion of the BVS in 2 patients having control OCT after 4 weeks after primary PCI. We can speculate that this was caused by the thrombus dissolution at the level of culprit lesion. Other possible explanation is the increase in distal mean reference diameter and area of the infarcted vessel during the follow-up. Nevertheless, the percentage of ISA was in general very low. At baseline or during the follow-up, much more less than 5 % of ISA per patient, which signify important stent malapposition, was detected [9, 12]. Furthermore, the percentage of late ISA in this study was similar to that in others that evaluated the effect of implanted BVS in stable patients. Gomez-Lara observed an ISA of 1 and 2.2 % struts at 6 months and 1 year after BVS implantation, respectively [4, 13]. Additionally, late ISA 1 year after implantation of different types of metal drug-eluting stents was 1.7–6.6 % [14]. Thus, the late ISA of BVS implanted in thrombotic lesions does not appear to be an issue or to influence patient outcomes. The very low rate ISA in presence of low rate of postdilatation in our study may be also explained by the systematic approach of BVS oversizing [9]. Postdilatation was performed only in two patients based on the finding of OCT with detection of strut ISA.

We observed advanced processes of neointimal coverage, even though coverage of BVS struts was assessed after only 4–6 weeks. Complete neointimal coverage was seen in two patients during OCT evaluation 6 months after BVS implantation. These findings of early BVS neointimal coverage confirm previous results [1, 4]. Only 1.6 % of struts were not covered after 6 months in the study by Gomez-Lara [4]. No difference in terms of the neointimal response was observed by OCT compared with metallic everolimus-eluting stents [13]. Regarding first generation drug-eluting stents, 19.8 % of sirolimus-eluting stent struts were uncovered during the follow-up in the study of Ikuta [15].

Strut discontinuity was not observed in the baseline OCT measurements after primary PCI; however, it was seen in two patients during the follow-up. Postdilatation at 16 atmospheres with a non-compliant balloon during the acute phase was performed in both cases. Discontinuity was seen in only two consecutive frames in each patient, and no treatment intervention was necessary. A morphological description of signs of OCT-discontinuity during the acute or early stages after BVS implantation was reported previously and is not rare [1, 5, 16]. Ormiston observed strut discontinuities in one-third of patients [1]. None of

these patients experienced MACEs, and all of them had discontinued their dual-antiplatelet therapy at 13 months.

One limitation of our study was the small number of patients. However, this report represents the only controlled OCT study performed in patients previously treated with BVS during the primary PCI. Secondly, in the majority of patients, OCT was performed soon after primary PCI. A longer-time period (>1 month) after BVS implantation would probably be best for evaluating late apposition and neointimal coverage. On the other hand, the timing of OCT was based on the timing of the staged PCI of the non-infarct artery with severe stenosis, and it would have been unwise to postpone this procedure. Thirdly, measurements of neointimal coverage thickness are not reported.

Conclusion

In this small study, persistent apposition and early neointimal coverage after biodegradable vascular scaffold implantation in patients with acute ST-segment elevation myocardial infarction were observed. The findings suggest a potentially good healing response after BVS implantation when BVS are used in this clinical setting that needs to be confirmed by larger-scale observations.

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Conflict of interest V. K. and P. W. received occasional speaker honoraria from Abbott Vascular. Other authors have no conflicts of interests to declare.

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