Insights from 2D and 3D Quantitative Angiographic Assessment of Bioresorbable Everolimus-Eluting Vascular Scaffolds

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ABSTRACT: **Background:** Bioresorbable vascular scaffold (BVS) is a promising technology that potentially offers several advantages over contemporary coronary drug-eluting stents (DES). Crucial to BVS implantation is the correct choice of scaffold size (diameter and length) in order to avoid "geographic miss" in length, provide the maximal support to the vessel wall, and avoid leaving "free-floating" foreign material in the coronary vasculature.

Objectives: To assess the optimal method for measuring coronary stenosis prior to BVS implantation.

Methods: We compared the performance of two quantitative coronary angiography assessment (QCA) techniques: two dimensional real-time QCA (2D-QCA) and offline 3D QCA (3D-QCA) for the evaluation of coronary lesions in patients enrolled in a multicenter randomized controlled trial of BVS vs. metallic stents, by calculating the weighted kappa value for agreement regarding optimal BVS size with the reference method – CoreLab offline 2D-QCA measurements. In addition, we collected 2 year clinical outcomes (death/myocardial infarction/repeat revascularization/scaffold thrombosis) in BVS-implanted patients.

Results: In 17 patients with available CoreLab data, the weighted kappa for agreement for 3D-QCA was significantly better than for 2D-QCA (0.90, 95%CI 0.72–1.00 vs. 0.439, 95%CI 0.16–0.77). The rate of clinical events at 2 years was low (9.5%).

Conclusions: Initial experience in a small group of carefully selected patients at our institution suggests that the use of BVS for coronary revascularization is associated with a low rate of adverse events in suitable patients. 3D-QCA may be superior to 2D-QCA analysis in terms of reproducibility, and results in more patients receiving optimal size BVS.

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KEY WORDS: bioresorbable vascular scaffold (BVS), quantitative coronary angiography (QCA), stents, vessel sizing

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Over the last decade, advances in coronary stents design improved the outcomes of percutaneous coronary interventions (PCI) [1,2]. However, drug-eluting stents (DES) are still associated with some degree of restenosis and with late and very late stent thrombosis [3,4]. Bioresorbable vascular scaffold (BVS) is a promising technology that potentially offers several advantages over contemporary coronary DES. BVS provides a temporary scaffold to prevent early recoil, constrictive remodeling and restenosis. However, unlike a metallic stent, it eventually resorbs over time and leaves no foreign material in the coronary vessel [5]. BVS also elutes anti-proliferative drugs to prevent restenosis while potentially reducing the risk of stent thrombosis similar to conventional DES. Serruys et al. [6,7] recently published the long-term results of a multicenter trial examining the efficacy and safety of BVS. They reported a low rate of clinical coronary end-points and excellent results with regard to various imaging studies used to assess the lumen dimensions and restenosis at 3 years.

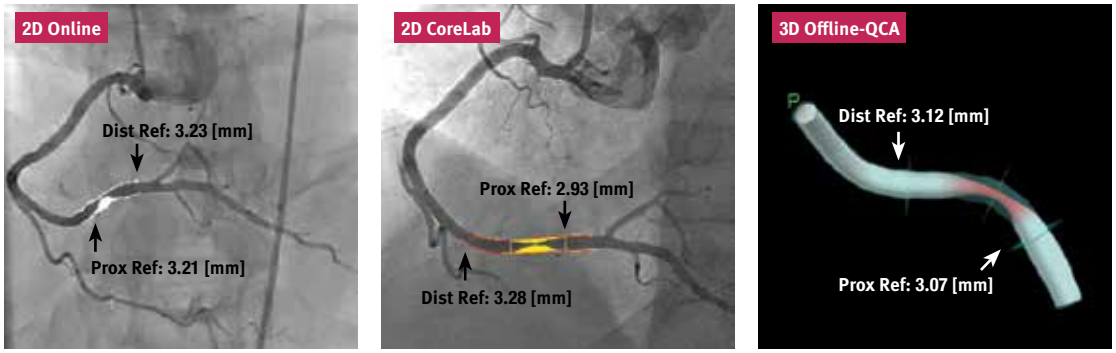
Crucial to BVS implantation is the correct choice of scaffold size (diameter and length). Optimal sizing is needed to avoid "geographic miss" in length in order to allow the BVS to provide the maximal support to the vessel wall and avoid the risk of leaving "free-floating" foreign material in the coronary vasculature.

In the current work, we attempted to define the optimal angiographic measurement technique for BVS sizing by comparing the agreement rate for BVS size selection of two- or three-dimensional (2D/3D) quantitative coronary angiography (QCA) assessment methods with the reference standard – namely, CoreLab 2D-QCA measurements.

PATIENTS AND METHODS

Twenty-one patients were treated with the Absorb® scaffold (Abbott Vascular, CA, USA) at the Rabin Medical Center according to conventional PCI indications. All patients participated in either the ABSORB II (N=8) or ABSORB-

Figure 1. Example of the different QCA analysis methods used in 17 patients: Online 2D-QCA (left), offline CoreLab 2D-QCA (middle), and offline 3D-QCA (right) analysis of the diameters of a distal RCA coronary lesion



RCA = right coronary artery, QCA = quantitative coronary angiography assessments

EXTEND (N=13) trials. Both trials were monitored by the Cardialysis Core Laboratory (Rotterdam, The Netherlands).

LESION MEASUREMENTS AND BVS SIZING

Coronary angiography was performed in all patients, and the decision whether the coronary lesion is suitable for BVS implantation was based on visual vessel-sizing assessment. The lesions intended for BVS implantation were then assessed by real-time 2D-QCA to measure their length and diameter. Once measured, the appropriate device size was chosen according to the specification of the ABSORB implantation protocol, based on the closest match between lesion and scaffold dimensions. All angiograms were reviewed and re-measured by the CoreLab using offline 2D-QCA. For this study, we performed an offline 3D-QCA reconstruction of the target vessel and lesion using the CardiOp-B system (Paieon Medical Ltd., Israel) [8,9].

In all cases, the technical operator performing the new 3D-QCA measurements was blinded to the original site and CoreLab 2D-QCA analysis results.

For the 3D-QCA measurement, proximal and distal reference diameters were selected in each of two orthogonal projections and the minimal lumen area was detected on each of the two 2D images. 3D reconstruction of the vessel was presented and the proximal and distal markers were used to measure the reference diameter and length of the region of interest [Figure 1].

CLINICAL FOLLOW-UP

All patients were contacted by telephone 1 month after discharge and were invited for outpatient clinic follow-up visits at 6 months, 1 year and 2 years post-scaffold implantation. In addition, at each time point the patient's electronic medical file was reviewed, and all major adverse cardiovascular and cerebrovascular events (MACCE, defined as death/myocardial infarction/repeat revascularization/scaffold thrombosis) during the follow-up period were recorded and adjudicated by physicians not involved in the trial.

STATISTICAL ANALYSIS

After completing all sets of measurements, we determined the agreement rate between the site and CoreLab regarding the optimal BVS size (per trial protocol for BVS size selection) for each QCA technique (2D and 3D). We then calculated the weighted kappa value for agreement with CoreLab 2D-QCA analysis (which served as the reference standard) for each QCA method.

RESULTS

Patients' demographic, clinical and angiographic characteristics are presented in Table 1. The average age was 59.8 years with male predominance; 80% presented due to acute coronary syndrome, 57% underwent prior PCI and 14% had previously undergone coronary artery bypass graft (CABG) surgery. The average stenosis degree was 83%, lesion length was 11.65 ± 3.5 mm, scaffold length 18.65 ± 3.5 mm and diameter 3.0 ± 0.28 mm (all measurements according to online measurements during the angiography). Target vessel was the left circumflex artery in 58%, right coronary artery in 23% and left anterior descending artery in 19% of the treated vessels. At 2 years follow-up, there were only two MACCE events (9.5%): two patients required a repeat revascularization – one (4.7%) due to scaffold thrombosis that resulted in myocardial infarction, and one (4.7%) underwent revascularization of a de novo lesion in a non-BVS-implanted coronary artery that manifested as unstable angina. All patients survived to 2 years follow-up.

ANGIOGRAPHIC ASSESSMENT AND BVS SIZE SELECTION

The ABSORB protocol for scaffold size selection is presented in Table 2. A complete set of measurements (online 2D-QCA, CoreLab 2D-QCA and offline 3D-QCA) was available for 17/21 patients. The various measurements of all 17 lesions and the eventual BVS size chosen are presented in Figure 2. Overall, online 2D-QCA assessment tended to result in larger estimates of the coronary lesion diameter compared to CoreLab 2D-QCA analysis,

Table 1. Demographic clinical and angiographic characteristics

Demographic and clinical characteristics	n=21
Age (years)	59.8 ± 10
Male	95
Current smoker	42
Dyslipidemia	85
Obesity	66
Ejection fraction (%)	57 ± 6
Previous MI	42
Previous PCI	57
Previous CABG	14
ACS	80
Angiographic characteristics	
LAD	19
RCA	23
Left circumflex	58
Degree stenosis (%)	83 ± 9
Average lesion length (mm)	11.65 ± 3.5
Proximal diameter (mm)	2.7 ± 0.25
Distal diameter (mm)	2.75 ± 0.32
Average BVS diameter (mm)	3.0 ± 0.28
Average BVS length (mm)	18.65 ± 3.5

Values are presented as number (%) or mean ± standard deviation

ACS = acute coronary syndrome, BVS = bioresorbable vascular scaffold, CABG = coronary artery bypass graft surgery, LAD = left anterior descending artery, MI = myocardial infarction, PCI = percutaneous coronary intervention, RCA = right coronary artery

whereas offline 3D-QCA tended to result in smaller estimates of coronary lesion diameter compared to CoreLab 2D-QCA analysis.

AGREEMENT BETWEEN 2D AND 3D QCA ANALYSIS

Agreement between 2/3D-QCA measurements and CoreLab analysis with regard to the appropriate BVS size is presented in Figure 2. The agreement rate of online 2D-QCA with the CoreLab analysis was 64.7% (11/17 patients). In all cases of disagreement the online analysis indicated the need for implantation of a larger BVS size than would have been selected according to the CoreLab analysis. The agreement rate of offline 3D-QCA with the CoreLab analysis was 94.1% (16/17 patients). For five of the six cases in whom there was disagreement between the site and CoreLab 2D-QCA analysis, it would have been resolved by using 3D QCA and no new disagreement would have occurred using the 3D-QCA analysis. The weighted kappa value for agreement with CoreLab analysis was 0.439 [95% confidence interval (CI) 0.16–0.77] for 2D-QCA and significantly improved to 0.90 (95%CI 0.72–1.00) with 3D-QCA ($P < 0.001$).

DISCUSSION

In this study we summarize our experience using BVS regarding two aspects: (i) the 2 year clinical outcomes following BVS implantation, and (ii) a comparison of different QCA methods for choosing the optimal BVS size. This is the first report from an Israeli center concerning BVS results and one of the first measured QCA reports in terms of 3D versus 2D analysis.

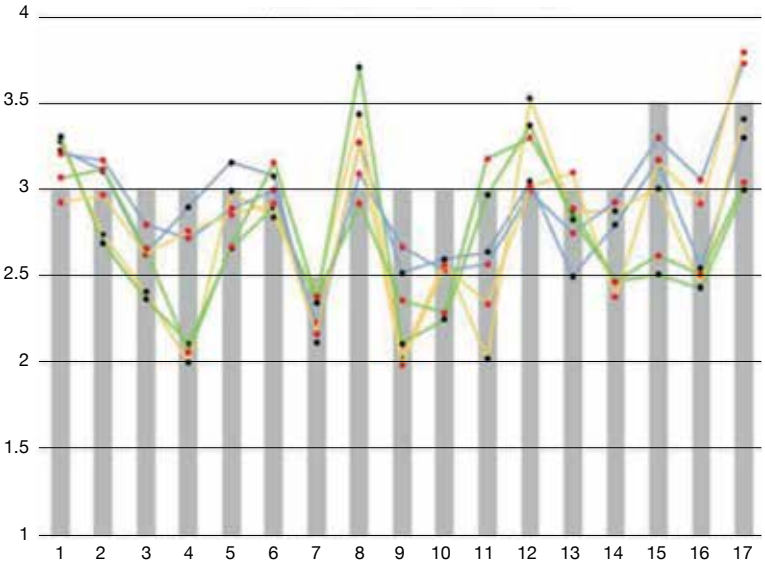
In terms of clinical outcomes, we observed a low rate of adverse cardiac events with the use of BVS in a carefully selected group of patients. With regard to QCA assessment, the weighted kappa value for agreement of the online 2D-QCA analysis with the Core Laboratory analysis was moderate at best, resulting in almost half the patients receiving oversized BVS. Our results suggest that using 3D-QCA analysis would have increased the kappa value significantly and all but one of the patients could

Table 2. Optimal BVS size according to lesion characteristics*

Target vessel diameter (distal and proximal ref) Ref	Target lesion length	Optimal BVS size
≥ 2.0 mm and ≥ 3.0 mm	≥ 14 mm	Single 2.5 x 18 mm
	> 14 mm and ≤ 22 mm	Single 2.5 x 28 mm
	> 22 mm and ≤ 28 mm	Two overlapping 2.5 x 18 mm
≥ 2.5 mm and ≥ 3.3 mm	≥ 14 mm	Single 3.0 x 18 mm
	> 14 mm and ≤ 22 mm	Single 3.0 x 28 mm
	> 22 mm and ≤ 28 mm	Two overlapping 3.0 x 18 mm
≥ 2.0 mm and ≥ 3.0 mm (distal) ≥ 2.5 mm and ≥ 3.3 mm (proximal)	> 22 mm and ≤ 28 mm	Two overlapping 3.0 x 18 mm

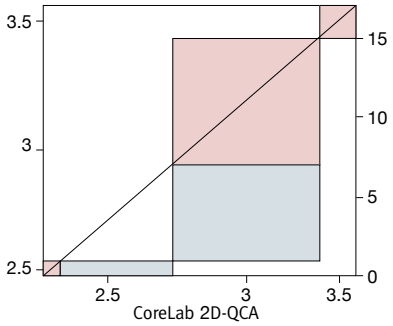
*According to the ABSORB and ABSORB – EXTEND trial protocols

Figure 2. BVS size. **[A]** QCA measurements and BVS size (n=17): proximal and distal lesion diameter according to the various QCA methods (colored dots) and corresponding BVS size (gray bars) for each patient

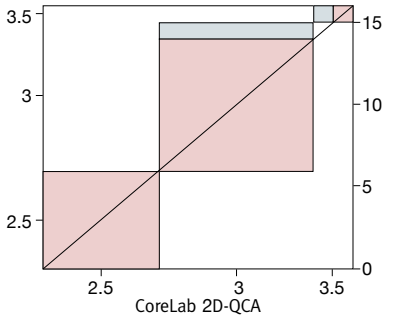


BVS = bioresorbable vascular scaffold, QCA = quantitative coronary angiography assessments

Figure 2. [B] Agreement with CoreLab regarding optimal BVS size according to QCA measurement method: online 2D-QCA (top panel) offline 3D-QCA (bottom panel)



Online 2D-QCA				
2D CreLab QCA	BVS size	2.5	3	3.5	
	2.5	1	6		7
	3		8		8
	3.5			2	2
		1	14	2	**11**



Offline 3D-QCA				
2D CreLab QCA	BVS size	2.5	3	3.5	
	2.5	6	1		7
	3		8		8
	3.5		1	1	2
		6	10	1	**15**

BVS = bioresorbable vascular scaffold, QCA = quantitative coronary angiography assessments

have received a more accurately sized BVS. Due to the importance of selecting the optimal size for BVS and the possible detrimental effects of implanting under- or oversized scaffolds, our results suggest that the 3D-QCA method is superior to 2D-QCA and may result in better BVS size selection. Nonetheless, our observation can only be viewed as hypothesis-generating considering the small sample size and hence low number of clinical events, which prevented evaluation of the possible clinical implications resulting from choosing suboptimal BVS size. It was previously reported that a 3D-reconstruction algorithm of coronary vessels and 3D-QCA analysis offers higher accuracy when compared with 2D-QCA, regardless of vessel type and lesion classification [8-12]. The 3D reconstruction improves visualization and may provide better diagnostic information than the 2D images of coronary lesions. Assessment of the lesion diameter and length are crucial for the purpose of device selection when using a BVS. Thus, 3D-QCA may provide a more precise analysis by overcoming the 2D display of a 3D structure and by avoiding foreshortening effects [13].

Since the use of BVS holds great promise and is expected to expand rapidly in the near future, we believe that our preliminary findings should provoke a discussion as to the best sizing method for BVS implantation. Specifically, 3D-QCA methods and/or intracoronary ultrasonic or optical imaging methods may be required over time to optimize BVS size selection and hence clinical outcomes [14].

LIMITATIONS

Our study has several limitations: first, it was a single-center study with a small sample size. Second, the better agreement of the 3D-QCA with the Core Laboratory measurements could stem from the fact that the 3D-QCA analysis was performed offline (like the Core Laboratory analysis) unlike the 2D-QCA performed online during the PCI procedure. Third, center-specific issues such as the experience and training of the technicians/interventional cardiologists could have affected and/or biased our results. Fourth, we did not compare QCA with other modalities such as intravascular ultrasound or optical coherence tomography, which may be better suited for choosing BVS size. It is worth remembering that 3D-QCA was previously reported as having a good agreement with intravenous ultrasound in assessment of left main artery dimensions [15].

CONCLUSIONS

Initial experience with a small group of patients at our institution suggests that the use of BVS for coronary revascularization is associated with a low rate of adverse events in a carefully selected patient population. 3D-QCA may be superior to 2D-QCA analysis in terms of reproducibility and results in more patients receiving optimal size BVS. Further trials with a larger sample size and multiple measurement modalities are necessary to find the optimal method of choosing BVS size.

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