

Relation between coronary plaque calcium deposits as described by computed tomography coronary angiography and acute results of stent deployment as assessed by intravascular ultrasound

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Abstract

Introduction: The findings from intravascular ultrasound studies on the impact of calcium deposits on the results of stent implantation are conflicting.

Aim: To evaluate whether calcium deposits as assessed by (CTCA) influence results of stent deployment.

Material and methods: The study population comprised 60 patients (43 male; age 64.2 ±8.6 years) who underwent CTCA before stent implantation. Lesion calcium score, total calcium length, and maximal area and maximal thickness of calcium deposits within the lesion segment were assessed. Plaques were divided into those with calcium score ≥ median (group 1), calcium score < median (group 2), and without calcium (group 3). Intravascular ultrasound (IVUS) was performed after attainment of optimal angiographic results of the stent procedure. Focal and diffuse stent expansion was defined as either minimum stent area (MSA) or mean stent area over the length of the stent divided by reference lumen area.

Results: The proximal reference segments of lesions with higher calcium score contained a larger plaque burden (47 ±12% vs. 41 ±9% vs. 34 ±18%, $p = 0.02$) – respectively for groups 1, 2, and 3. Positive correlation was observed between lesion calcium score and frequency of post-dilation ($R = 0.28$, $p = 0.03$). There was no difference in focal stent expansion (71 ±14% vs. 65 ±15% vs. 71 ±15%, $p = 0.3$) or diffuse stent expansion (92 ±30% vs. 85 ±30% vs. 93 ±38%, $p = 0.7$) comparing groups 1, 2, and 3. Lesion calcium score, total length of calcium, and maximum area and thickness of calcium deposits did not correlate with focal or diffuse stent expansion.

Conclusions: Lesions with a higher CTCA calcium score had larger reference plaque burden after stent implantation and more likely required post-dilation, but final stent expansion as assessed by IVUS was not affected by the amount of CTCA calcium provided an angiographically optimal result was achieved.

Key words: computed tomography coronary angiography, calcium deposits.

Introduction

The findings from previous intravascular ultrasound studies on the relation between calcium deposits and results of stent deployment are conflicting [1-3]. Computed tomography coronary angiography (CTCA) allows detailed assessment of coronary plaque calcium including the features that cannot be quantified by intravascular ultrasound (IVUS): area and thickness of calcium deposits.

Aim

The aim of our study was to evaluate whether presence and quantitative characteristics of calcium deposits

within coronary lesion as assessed by CTCA may influence the results of stent deployment evaluated with IVUS.

Material and methods

The current study was a post-hoc analysis of the results of a single center randomized study with IVUS endpoints [4]. The protocol of the initial study has been registered at ClinicalTrials.gov (NCT01205425). The detailed inclusion and exclusion criteria have been published [4]. All patients included in the current analysis underwent coronary stent implantation and IVUS examination after the operator confirmed an optimal angiographic outcome

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of the procedure defined as a residual stenosis < 30% by visual estimation. The study was approved by the local Ethics Committee and was performed in accordance with the Helsinki II Declaration. All participating patients signed informed consent. We included consecutive patients with stable coronary artery diseases who underwent CTCA as the first anatomical evaluation of coronary arteries prior to invasive coronary angiography. The major inclusion criterion was the presence of at least one single significant (> 70% stenosis) CTCA coronary lesion in a native coronary artery likely to undergo percutaneous coronary intervention (PCI).

Prior to contrast enhanced CTCA a native scan was performed for the assessment of the calcium score (expressed as Agatston Score Equivalents [ASE]). Quantification of coronary calcifications was performed using dedicated software for post-processing (Syngo Multimodality Workplace™, Siemens, Forchheim, Germany). An experienced observer (JJ) blinded to the IVUS data analyzed the calcium score scan in relation to the coronary angiogram recorded during percutaneous coronary intervention (PCI). Then the value of the calcium score confined to the stented segment (lesion calcium score) was assessed to quantify the lesion-specific calcium deposits (Figure 1). Lesions were divided into three groups: no calcium, lesion calcium score < median, and lesion calcium score ≥ median.

The contrast enhanced CTCA dataset was acquired with a dual-source CT scanner (Somatom Definition, Siemens, Forchheim, Germany) after sublingual administration of nitrates (0.8 mg). The CTCA data were analyzed off-line with quantitative CT software (Circulation®, Siemens, Forchheim, Germany). Images were displayed with a visu-

ally adjusted setting and were analyzed by an experienced observer (JJ) simultaneously with the coronary angiogram. To differentiate calcium deposits from the contrast medium the scout scan was compared with the contrast enhanced CTCA. Several parameters featuring calcifications within the stented segment were measured: total length of all calcium deposits, maximal calcium area in a single cross-section, and maximal calcium thickness at the site of maximal calcium area (Figure 2).

The IVUS was performed after attaining optimal angiographic results. Intracoronary nitroglycerine (0.2 mg) administration was performed, and the IVUS catheter (Volcano Corporation, San Diego, California, USA) was advanced > 10 mm distal to the stented segment; and imaging was performed retrograde with an automatic pullback (0.5 mm/s). Off-line IVUS analyses were performed by an observer (JP) blinded to the CTCA findings and according to the established criteria [5]. Planimetric IVUS measurements were performed at the minimal stent area (MSA) site and at the proximal and distal reference sites defined as the largest lumen area located within 10 mm long segments adjacent to the stent shoulders, but before a major side-branch. Volumetric assessment of the stented segment was performed every 1 mm to calculate the mean stent area. Reference measurements included lumen and external elastic membrane (EEM) areas; plaque burden was calculated according to the formula: $[(EEM \text{ area} - \text{lumen area})/EEM \times 100\%]$. Focal stent expansion was defined as the MSA divided by mean reference lumen area. Diffuse stent expansion was defined as mean stent area divided by the mean reference lumen area. Quantitative IVUS findings including

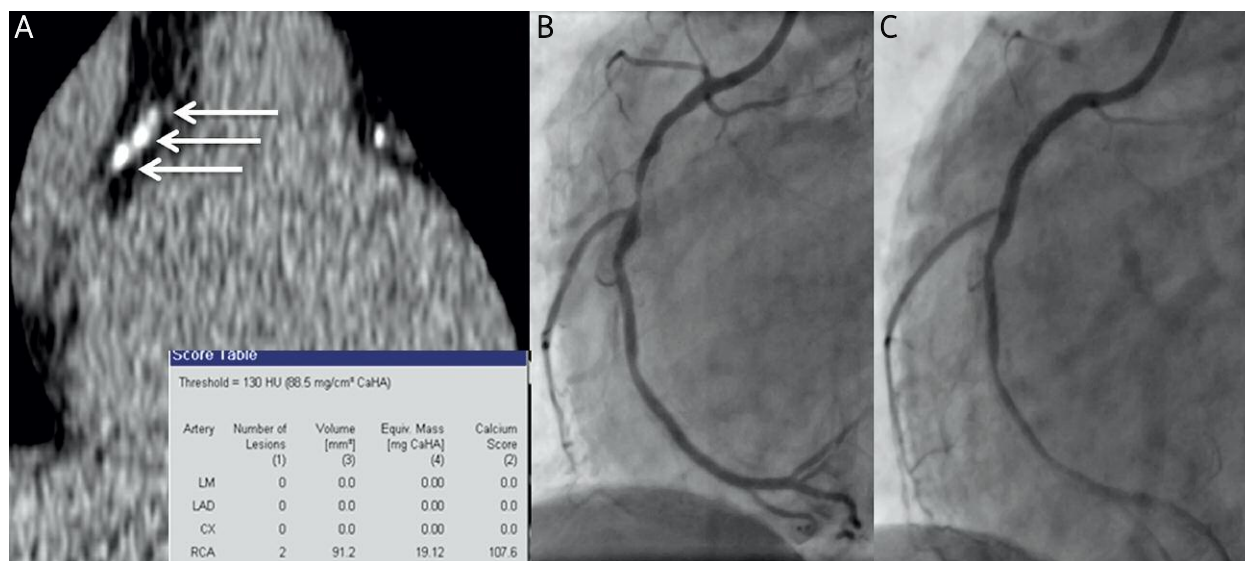


Fig. 1. The lesion calcium score scan in relation to the coronary angiogram recorded during PCI. **A** – Scout CT scan performed for the evaluation of calcium score. Arrows indicate calcium deposits located within the target lesion in the right coronary artery (lesion calcium score: 107.6). **B** – Coronary angiography with significant lesion at the location of calcium deposits in mid right coronary artery. **C** – Right coronary artery after stent implantation

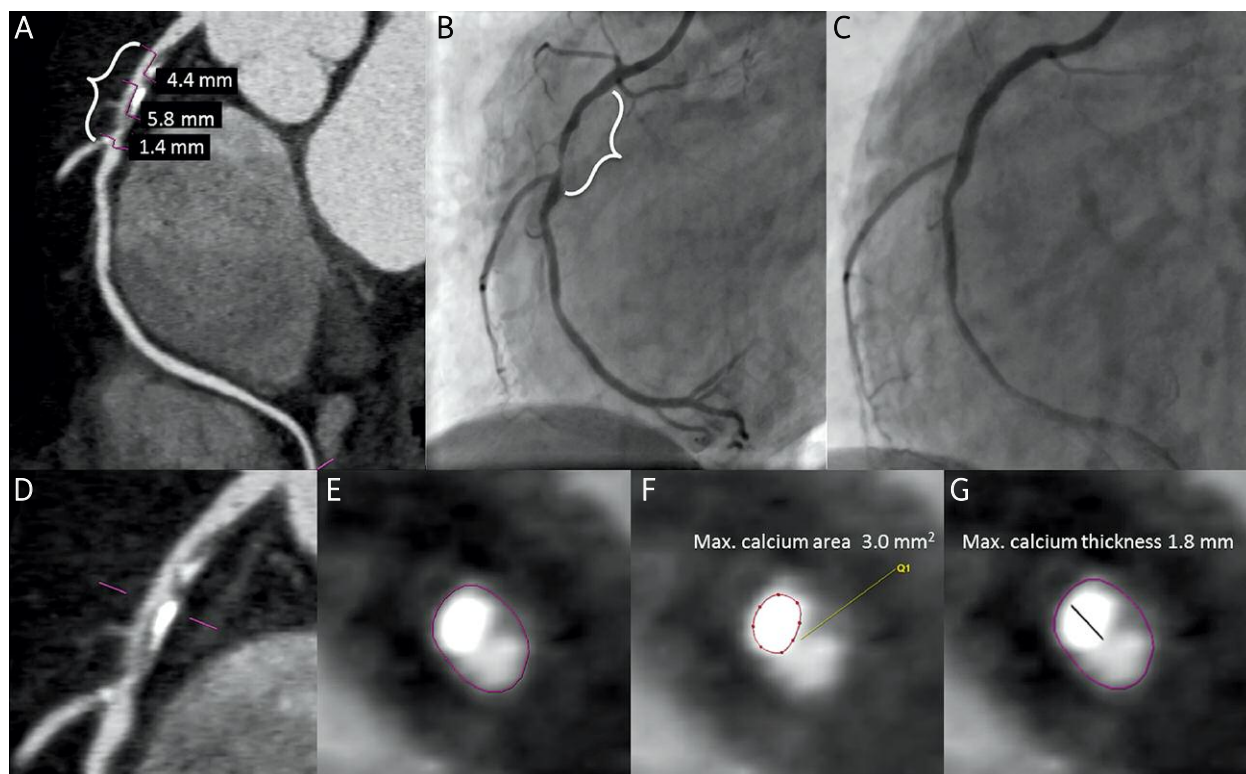


Fig. 2. Calcium measurements within the coronary lesion detected by CTCA. **A** – Curved multiplanar reconstruction of RCA with significant stenosis; three separate calcium deposits were identified within the lesion (total length: 11.6 mm). **B** – The cineangiogram of RCA with stenosis initially detected by CTCA. **C** – RCA after stent implantation. **D** – Curved multiplanar reconstruction of RCA focused on the lesion site. **E** – The cross-section located within the target lesion with maximal area and thickness of calcium. **F** – Measurement of maximal area of calcium (3.0 mm²). **G** – Measurement of maximal calcium thickness (1.8 mm)

presence of stent malapposition, tissue prolapse, and stent edge dissection were identified according to established criteria [6-8].

Statistical analysis

Continuous data with normal distribution are presented as means with standard deviation while the non-normally distributed variables are presented as medians with interquartile ranges (IQR). An independent samples *t*-test, one-way ANOVA or Mann-Whitney test was used to assess differences between continuous variables. Categorical variables were compared with χ^2 test. Correlations of continuous variables were assessed with the Spearman test. We used MedCalc version 9.3.8.0 (Mariakerke, Belgium) for statistical analyses.

Results

The study population comprised 60 patients in whom 64 separate coronary lesions were treated with stent implantation between September 2009 and April 2011. Paired native scan for calcium score assessment and contrast enhanced CTCA were available for 60 lesions (94%); this group is the basis for all analyses performed. The medi-

an time between CTCA and stent implantation was 30 (14.5-47.5) days. Calcium deposits were identified in 47 (78%) lesions. In lesions containing calcium deposits, the median calcium score was 60.2 (10.9-152.2), median length of the calcium deposits was 7.5 (3.9-10.9) mm, median maximal calcium area was 3.1 (1.8-5.0) mm², and median maximal calcium thickness was 1.5 (1.3-1.8) mm.

Baseline demographic, clinical and procedural variables of the study patients divided into groups according to the lesion calcium score are presented in Table 1. There was no significant difference between maximal balloon pressure during stent implantation into lesions without calcium, lesions with calcium score < median, and lesions with calcium score \geq median (15.2 \pm 2.9 atm vs. 16.1 \pm 2.6 atm vs. 16.8 \pm 2.9 atm, $p = 0.2$). However, we observed a correlation between maximal calcium cross-sectional area within the stented segment and the maximal balloon pressure applied to achieve optimal angiographic results ($R = 0.32$, $p = 0.01$). Moreover, in order to obtain optimal angiographic results, stent post-dilation tended to be more often required in lesions with a higher calcium score: 9 (38%) vs. 4 (17%) vs. 1 (8%), $p = 0.09$, respectively, for lesions with calcium score \geq median, lesions with calcium

Table 1. Baseline demographic, clinical and procedural variables with regards to the lesion calcium score

Variable	Lesion calcium score = 0 (n = 13)	Lesion calcium score < median (n = 23)	Lesion calcium score ≥ median (n = 24)	Value of p
Male, n	9	16	14	0.6
Age [years], mean ± SD	62.8 ± 6.9	64.2 ± 8.5	65.9 ± 9.0	0.6
Diabetes mellitus, n	3	5	3	0.7
Hypercholesterolemia, n	11	20	21	0.5
Hypertension, n	11	21	21	0.5
Location of target lesion, n				0.5
LAD	4	16	14	
LCX	3	2	2	
RCA	6	5	8	
Nominal stent diameter [mm]	3.2 ± 0.4	3.2 ± 0.5	3.1 ± 0.4	0.9
Maximal balloon pressure [atm]	15.2 ± 2.9	16.1 ± 2.6	16.8 ± 2.9	0.2
Length of the stented segment [mm]	21.0 ± 8.4	19.8 ± 4.8	23.5 ± 7.6	0.15
Number of stents/lesion	1.1 ± 0.3	1.1 ± 0.3	1.0 ± 0.2	0.5
Direct stenting, n	9	18	13	0.2
Post-dilation, n	1	4	9	0.09

LAD – left anterior descending artery, LCX – left circumflex artery, RCA – right coronary artery, hypercholesterolemia was defined as LDL level > 3.0 mmol/l or the patient was on statin therapy prior to CTCA scan (after CTCA all patients with diagnosed significant stenosis received statin), hypertension was defined as blood pressure ≥ 140/90 mm Hg or the patient was receiving antihypertensive treatment

score < median, and lesions without calcium. A positive correlation was observed between increasing lesion calcium score and frequency of post-dilation ($R = 0.28$, $p = 0.03$).

Calcium containing lesions were located in larger vessels as indicated by the difference in the proximal reference EEM area ($18.2 \pm 4.5 \text{ mm}^2$ vs. $19.8 \pm 5.9 \text{ mm}^2$ vs. $14.4 \pm 4.3 \text{ mm}^2$, $p = 0.03$, respectively, for lesions with calcium score ≥ median, lesions with calcium score < median, and lesions without calcium). With increasing lesion site calcium, we observed a larger plaque burden in the reference segments adjacent to the proximal stent edge ($p = 0.02$) (Table 2).

The MSA and mean stent area were similar regardless of the magnitude of lesion calcium (Table 2). The percentage of lesions with MSA < 4.5 mm^2 did not differ between the groups: 6 (25%) vs. 6 (26%) vs. 3 (23%), $p = 0.9$, respectively for lesions with calcium score ≥ median, lesions with calcium score < median, and lesions without calcium. Total length of calcium deposits, maximal calcium area, and thickness did not affect MSA (Table 3). There was no significant difference in focal stent expansion between lesions categorized according to their calcium score: $71 \pm 14\%$ vs. $65 \pm 15\%$ vs. $71 \pm 15\%$, $p = 0.3$, respectively, for lesions with calcium score ≥ median, lesions with calcium score < median, and lesions without calcium. Also, we did not observe correlations between focal stent expansion versus lesion calcium score or other CTCA parameters quantitatively describing calcium deposits (Table 4). Diffuse stent expansion was similar in all 3 lesion subgroups: $92 \pm 30\%$ vs. $85 \pm 30\%$ vs. $93 \pm 38\%$, $p = 0.7$, respectively, for lesions with

calcium score ≥ median, lesions with calcium score < median, and lesions without calcium. The lesion calcium score, total length of calcium deposits, and maximal calcium area and thickness did not correlate with diffuse stent expansion (Table 4).

Frequency of acute stent malapposition (3 (13%) vs. 4 (17%) vs. 3 (23%), $p = 0.7$), tissue prolapse (5 (21%) vs. 2 (9%) vs. 1 (8%), $p = 0.2$) and stent edge dissections (3 (13%) vs. 1 (4%) vs. 1 (8%), $p = 0.5$) (respectively for lesions with calcium score ≥ median, lesions with calcium score < median, and lesions without calcium) were similar in all 3 lesion subgroups.

Discussion

The main findings of the current study were as follows. The presence and magnitude of calcium identified by CTCA were not related to the final stent expansion. Reference segments adjacent to the stent edges contained a larger plaque burden in lesions with a larger amount of calcium. Lesions with more extensive calcifications by CTCA more likely required post-dilation and higher balloon pressures before optimal angiographic results were obtained.

The CTCA is a non-invasive imaging modality that allows assessment of both the vessel lumen and coronary plaque composition and, especially, accurate quantification of calcium deposits sharing some features of IVUS [9]. Moreover, due to signal loss behind the leading edge of calcified plaque, IVUS may not evaluate the total area and thickness of calcium, which can be relatively easily quantified by CTCA. Moreover, plaque composition as

Table 2. Comparison of IVUS findings after stent implantation in lesion with regards to the lesion calcium score

Variable	Lesion calcium score = 0 (n = 13)	Lesion calcium score < median (n = 23)	Lesion calcium score ≥ median (n = 24)	Value of p
Minimal stent area [mm ²]	6.1 ±2.2	6.4 ±2.4	6.1 ±1.7	0.9
Mean stent area [mm ²]	7.2 ±2.3	7.5 ±2.4	7.3 ±1.7	0.9
Proximal reference lumen area [mm ²]	9.5 ±4.4	11.5 ±3.7	9.7 ±2.9	0.18
Proximal reference EEM area [mm ²]	14.4 ±4.3	19.8 ±5.9	18.2 ±4.5	0.017
Proximal reference plaque burden [%]	34 ±18	41 ±9	47 ±12	0.02
Distal reference lumen area [mm ²]	8.2 ±3.4	8.6 ±3.1	7.9 ±2.2	0.7
Distal reference EEM area [mm ²]	12.7 ±4.1	14.5 ±5.6	13.4 ±4.3	0.5
Distal reference plaque burden [%]	33 ±11	38 ±16	39 ±14	0.5

EEM – external elastic membrane

assessed by CTCA may predict procedural complications such as myocardial infarction [10]. The current study examines the relation between plaque calcification by CTCA and the outcome of stent implantation by IVUS. Previous IVUS data on the possible relation between presence and extent of calcium deposits and stent expansion are conflicting. Albrecht *et al.* found that calcified lesions interfered with optimal stent deployment [1]. Vavuranakis *et al.* showed that stent expansion was inversely correlated with the extent of calcifications [2]. However, our results are in line with more recent IVUS analyses by Costa *et al.*, who found no relation between either calcium arc or length measured by pre-intervention IVUS and stent expansion [3]. Of note, mean focal stent expansion achieved in our study was approximately 70% and approximately 25% of lesions had an MSA below the threshold of 4.5 mm² despite optimal angiographic results. These findings are also in line with the study by Costa *et al.* and highlight the potential role of IVUS guidance during stent implantation even if angiographic results of the procedure look satisfactory.

We found a larger reference segment plaque burden in lesions with a higher calcium score. This is in line with reports from IVUS studies showing a positive correlation between calcium and plaque burden [11, 12]. However, as our study IVUS was performed only after stent implantation, we cannot exclude that a larger reference plaque burden was caused by larger plaque shifts after stent implantation into calcified lesions.

The results of studies by Kass *et al.* and LaBounty *et al.* and our previous reports showed that evaluation of lesion length and diameter derived from CTCA may beneficially influence stent size selection, procedure extent, and acute results as assessed by IVUS [4, 13-15]. Previous IVUS studies have also shown that a larger reference segment plaque burden was associated with increased risk of stent thrombosis [16]. Therefore, a higher lesion calcium score identified by CTCA may also influence the decision about IVUS guidance in order to ensure adequate lesion coverage. Our findings of positive correlations between maximal calcium area and maximal balloon pressure and

Table 3. Comparison of calcium deposit features according to the minimal stent area

Variable	Lesions with MSA < 4.5 mm ² (n = 15)	Lesions with MSA ≥ 4.5 mm ² (n = 45)	Value of p
Lesion calcium score	45.2 (3.3-165.0)	27.6 (3.7-78.3)	0.6
Total length of all calcium deposits [mm]	6.1 (2.0-10.0)	5.5 (2.0-11.0)	0.9
Maximal calcium area [mm ²]	2.2 (1.1-2.9)	2.8 (1.0-5.1)	0.3
Maximal calcium thickness [mm]	1.5 (1.0-2.0)	1.4 (1.0-2.0)	0.5

Table 4. Correlation between quantitative CTCA variables describing calcium deposits and measures of stent expansion by IVUS

Variable	Focal stent expansion [%]	Diffuse stent expansion [%]
Lesion calcium score	$R = -0.13, p = 0.3$	$R = -0.05, p = 1.0$
Total length of all calcium deposits [mm]	$R = -0.01, p = 0.9$	$R = 0.02, p = 0.9$
Maximal calcium area [mm ²]	$R = 0.06, p = 0.6$	$R = 0.04, p = 0.7$
Maximal calcium thickness [mm]	$R = -0.07, p = 0.6$	$R = -0.3, p = 0.8$

between lesion calcium score and frequency of post-dilation were also in line with the results of Vavuranakis *et al.* and further support the concept that CTCA data should be used, if available, for preliminary planning of the stent implantation procedure [2, 4].

The major limitation of our study was the relatively small sample size and the fact that the results may not apply to heavily calcified lesions.

Conclusions

Lesions with a higher calcium score had a larger reference plaque burden after stent implantation and were more likely to require post-dilation with higher balloon

pressure, but final stent expansion as assessed by IVUS was not affected provided an angiographically optimal result was achieved.

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