Platelet Aggregation on Optical Coherence Tomography after Rotational Atherectomy of Severely Coronary Calcified Lesions

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Cheng-fu CAO
Peking University People's Hospital

Yu-liang MA
Peking University People's Hospital

Qi LI
Peking University People's Hospital

Jian LIU
Peking University People's Hospital

Hong ZHAO
Peking University People's Hospital

Ming-yu LU
Peking University People's Hospital

weimin wang
Peking University People's Hospital

weiminwang@vip.sina.com

ORCiD: https://orcid.org/0000-0003-4953-0777

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Abstract

Background
Rotational atherectomy (RA) has improved percutaneous treatment of severe coronary calcified lesions, but the "no-reflow" phenomenon remains a serious complication. Platelet activation by RA may contribute to the no-reflow, we use OCT to test the effect of RA on platelet aggregation.

Methods
We analyzed 20 consecutive patients with severe coronary calcified lesions by OCT imaging performed before and after RA and after stent implantation.

Results
Mean burr size was 1.48 ± 0.14. Mean rotation speed was 152,300 ± 4,200 rpm. Mean number of rotations per patient was 5.3 ± 2.1 times and mean ablation time per RA was 11.3 ± 3.2 seconds. All the target vessels had platelet aggregation on OCT after RA. The average number of white thrombus per lesion after RA was 7.23 ± 4.4, and the average length of every white thrombus was 0.51 ± 0.33 mm. In Pearson Correlation Analysis, platelet aggregation load was related with burr size \( r = 0.575, P = 0.040 \) and rotation number \( r = 0.599, P = 0.031 \).

Conclusions
Platelet aggregation during RA is proved by OCT in vivo. The bigger burr size, higher number of ablation times, maybe together with higher rotation speed can influence the platelet aggregation load. These data suggest a proper RA strategy to avoid no-reflow during RA.

Background
Coronary calcification plaque is common in patients undergoing percutaneous coronary interventions (PCI), the incidence ranges between 17% and 35% [1]. Coronary calcification affects the surgery success rate and long-term clinical outcome [2, 3]. Calcified lesions can lead to stent implantation failure or incomplete stent expansion, thus affecting the long-term efficacy of stents. It also increases the risk of perforation and coronary dissection during operation [4, 5]. Rotational atherectomy (RA) plays a key role in the therapy of severe calcified lesions [6, 7]. It can facilitate successful stent delivery and expansion. Current guidelines recommend that RA is reasonable for heavily calcified lesions that cannot be crossed by a balloon or adequately dilated before stenting.

Platelet activation is an important determinant of acute outcomes of PCI. Some studies had confirmed
that RA can cause platelet aggregation in vitro models [8, 9], which lead to slow flow or no reflow during RA [10].

Optical coherence tomography (OCT) is a high resolution (10 um axial), light-based imaging modality, and is a commonly used intravascular imaging method to evaluate coronary plaque, which has been demonstrated to shown excellent correlation with histology [11]. To our knowledge, there has been no imaging study to assess the effect of RA on platelet activation by OCT. The purpose of this study was to use OCT to examine the effect of RA on platelet aggregation.

Methods
Study population
This is a single-center observational study, including 53 consecutive patients who underwent OCT imaging due to severe coronary calcification on angiography from July 2019 to December 2019. The definition of severe calcification on angiography was defined as clear calcified shadows can be seen in both beating and resting hearts before contrast injection. If OCT image shows maximum calcium angle > 180°, maximum calcium thickness > 0.5 mm and maximum calcium length > 5 mm, the patients will receive RA therapy before stent placement [12]. If the OCT catheter did not pass the lesion, OCT was performed immediately after dilation with a small balloon. Finally, 20 patients met the above criterion and were included in our study. The demographic and clinical characteristics of all patients were derived from electronic record system.

This study was approved by the ethics at Peking University People’s Hospital, all patients provided written informed consent before participation.

RA details
Before procedural, all patients received an oral loading dose of 300 mg aspirin and 600 mg clopidogrel. During procedural, all patients received unfractionated heparin at a dose of 70–100 U/kg or bivalirudin to maintain an activated clotting time (ACT) > 300 seconds. The choice of vascular access, burr size was left at the operators’ discretion. RA was performed by using the Rotablator (Boston Scientific Scimed, Inc., Maple Grove, MN, USA). The burr size was selected to reach a burr/vessel ratio of 0.5–0.6. RA speed ranged between 140,000 and 160,000 rotation per minute. Each ablation time was 10–15 seconds. During RA, A continuous intracoronary infusion of a cocktail
with unfractionated heparin and nitroglycerin was employed. Success of RA was defined as complete expansion of balloon of target lesion after RA.

**OCT Image Acquisition and Analysis**

OCT image acquisition was performed before RA, after RA and after stent placement with C7-XR or ILUIMEN OPTIS OCT Intravascular Imagining System (Abbott, USA). All OCT data were analyzed using Abbott Vascular Offline Review Workstation by two independent interventional cardiologists who were blinded to the clinical and angiographic information.

The minimum lesion lumen area (MSA) was defined as the smallest crosssectional area (CSA) in the lesion segment. Calcium lesion was evaluated using three parameters: maximum angle, maximum thickness, and length. When calcium was extremely thick and its border was not clear due to attenuation, the maximum visible thickness was measured [12].

Platelet aggregation was proved by OCT finding a mass attached to luminal surface or floating within the lumen, which is less backscattering, homogeneous, and has low attenuation (white thrombus) [13]. Thrombotic load was evaluated by the number of white thrombus on OCT.

**Statistical Analysis**

Descriptive statistics are presented as mean ± SD and compared with the t-test. Categorical data are expressed as frequency and percentage and compared with chi-square or Fisher exact test where appropriate. Pearson Correlation Analysis was used to analyze the correlation between continuous variables.

**Results**

**Patient Characteristics**

We finely included 20 consecutive cases, baseline clinical characteristics were summarized in Table 1.

The average age of the patients was 70.3 ± 9.5 years. Most patients were male (75%), and clinical manifestations were acute coronary syndrome (ACS).
Table 1
Baseline patients characteristics

| Characteristic                  | n = 20          |
|---------------------------------|-----------------|
| Age (years)                     | 70.3 ± 9.5      |
| Male gender, n (%)              | 14 (70%)        |
| Body mass index, (Kg/m²)        | 25.7 ± 4.2      |
| Hypertension, n (%)             | 12 (60%)        |
| Hyperlipidemia, n (%)           | 7 (35%)         |
| Diabetes mellitus, n (%)        | 11 (55%)        |
| Smoking, n (%)                  | 7 (35%)         |
| Prior PCI, n (%)                | 3 (15%)         |
| Prior CABG, n (%)               | 3 (15%)         |
| LDL-c (mmol/L)                  | 2.23 ± 1.02     |
| eGFR (ml/Kg.1.73 m²)            | 86.3 ± 12.9     |
| Type of CAD                     |                 |
| SA, n (%)                       | 5 (25%)         |
| UA, n (%)                       | 10 (50%)        |
| NSTEMI, n (%)                   | 5 (25%)         |

Details of RA and Stent Placement

Detailed information on RA techniques and stents placement data was shown in Table 2. The most common RA target vessel was left anterior descending branch (LAD), there was no left circumflex branch RA in our data. The most commonly employed burr size was 1.5 mm (70%), mean burr size was 1.48 ± 0.14. Mean rotation speed was 152,300 ± 4,200 rpm. Mean number of rotations per patient was 5.3 ± 2.1 times and mean ablation time per RA was 11.3 ± 3.2 seconds. The mean ACT time was 300.3 ± 35.7 seconds. There was only one patient with no reflow after RA.

Table 2
Details of RA and stent

|                        | n = 20 |
|------------------------|--------|
| Target Vessel          |        |
| LAD, n (%)             | 17 (85%)|
| LCX, n (%)             | 0      |
| RCA, n (%)             | 3 (15%)|
| Burr size (mm)         |        |
| 1.25 mm, n (%)         | 4 (20%) |
| 1.5 mm, n (%)          | 14 (70%)|
| 1.75 mm, n (%)         | 2(10%)  |
| Rotation speed (rpm)   | 15.2 ± 0.4|
| Rotation number (n)    | 5.3 ± 2.1|
| Ablation time per RA(sec) | 11.3 ± 3.2 |
| ACT time (sec)         | 300.3 ± 35.7|
| Slow flow/no reflow (n)| 1 (5%)  |
| Stent number (n)       | 1.94 ± 0.68|
| Total stent length (mm)| 57.5 ± 21.6|

Table 3
OCT Based Lesion Modification before and after RA

|                         | Before RA          | After RA          | P value |
|-------------------------|--------------------|-------------------|---------|
| Maximum calcium angle (°)| 322.5 ± 58.8       | 309.4 ± 63.6      | 0.919   |
| Maximum calcium thickness (mm) | 1.67 ± 0.27       | 0.86 ± 0.19       | 0.171   |
| Calcium length (mm)     | 41.7 ± 13.5        | 40.7 ± 13.3       | 0.719   |
| Minimal lumen CSA (mm²) | 1.35 ± 0.35        | 1.86 ± 0.29       | 0.157   |
| White thrombus (n)      | 0                  | 20                |         |
| Calcium crack (n)       | 0                  | 16                |         |
| Dissection (n)          | 0                  | 3                 |         |
OCT Based Lesion Modification before and after RA

OCT showed that the maximum calcium angle, maximum calcium thickness and calcium length was 322.5 ± 58.8° vs. 309.4 ± 63.6°, 1.67 ± 0.27 vs. 0.86 ± 0.19 mm, and 41.7 ± 13.5 vs. 40.7 ± 13.3 mm before and after RA respectively. Although the difference was not statistically significant, maximum calcium thickness was lower than pre-RA. We found that all the target vessels had white thrombus on OCT after RA, which was the evidence of platelet activation. This phenomenon was never reported before. Representative OCT images of RA-related white thrombus are shown in Fig. 1. RA led to calcium crack in 80% lesions and dissection in 15% lesions. Representative OCT images of calcium crack and dissection are shown in Fig. 2.

Impact Factors of RA-induced White Thrombus

OCT showed the average number of white thrombus per lesion after RA was 7.23 ± 4.4, and the average length of every white thrombus was 0.51 ± 0.33 mm. Pearson Correlation Analysis was used to analyze the correlation between thrombotic load (number of white thrombus) and other variables (burr size, rotation speed, rotation number, ablation time per RA, ACT, maximum calcium angle, maximum calcium thickness, calcium length and minimal lumen area). The result showed that the thrombotic load was related with burr size ($r = 0.575, P = 0.040$) and rotation number ($r = 0.599, P = 0.031$). Bigger burr size and higher number of rotation would result in higher thrombotic load.

Discussion

We reported first time OCT images of RA induced platelet aggregation of severe calcified coronary lesions.

RA played an important role in pre-treat of severe calcified lesions before stenting. Complications of RA included coronary dissection (10.5%), severe coronary spasm (1.6–6.6%), acute vascular occlusion (3.1%), slow-flow/no-reflow (1.2–7.6%) and coronary artery perforation (0–2%) [14.15]. Among these complications, no-reflow phenomenon remains serious and common. Potential mechanisms of no-reflow during RA included atheromatous debris embolism, platelet activation, microcirculatory vasospasm and so on [16]. Previous study had proved the effect of RA on platelet activation in an in vitro model [8]. To our knowledge, this is the first report about the effect of RA on platelet aggregation in vivo on OCT imaging. In Annapoorna S. Kini’s article which assessed of the mechanistic effects of
rotational and orbital atherectomy in severely calcified coronary lesions by OCT (RA details: burr size 1.68 ± 0.11, rotation speed 150,000 rpm) [17], the authors found the similar phenomenon, also in all the lesions treated by RA. They defined this phenomenon as small intimal nodules. But we still think it is white thrombus, due to the different transmissivity and the clear boundary from intima.

The load of platelet aggregation is influenced by several factors. In our study, we found bigger burr size and higher number of rotation would result in higher thrombotic load. In vitro model study, compared with high-speed RA (180,000 rpm), low-speed RA (140,000 rpm) can reduce the platelet aggregation [8]. In our study, we did not find the influence of rotation speed on platelet aggregation, the reason maybe that in our center we use low-medium rotation speed (140,000-160,000 rpm) in all the patients in clinical practice, so the relation of rotation speed and platelet aggregation can’t be found in the Pearson Correlation Analysis. These data suggest a proper RA strategy (burr size, rotation speed and ablation numbers) to avoid no-reflow during RA.

**Conclusions**

Platelet aggregation during RA is proved by OCT in vivo. The bigger burr size, higher number of ablation times, maybe together with higher rotation speed can influence the platelet aggregation load. These data suggest a proper RA strategy to avoid no-reflow during RA.

**List Of Abbreviations**

| Abbreviation | Description                      |
|--------------|----------------------------------|
| PCI          | percutaneous coronary interventions |
| RA           | rotational atherectomy            |
| OCT          | optical coherence tomography      |
| ACT          | activated clotting time           |
| CSA          | crosssectional area               |
| MSA          | minimum lesion lumen area         |
| LAD          | left anterior descending branch    |
| ACS          | acute coronary syndrome           |

**Declarations**

**Ethics approval and consent to participate**

This study was approved by the ethics at Peking University People’s Hospital, all patients provided written informed consent before participation.

**Consent for publication**

Not applicable

**Availability of data and materials**
The datasets used during the current study are available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors' contributions**

Cheng-fu CAO was a major contributor in writing the manuscript. Yu-liang MA and Qi LI analyzed and interpreted the patient data, Jian LIU, Hong ZHAO and Ming-yu LU collected the patients data, Wei-min WANG was the corresponding author. All authors read and approved the final manuscript.

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Not applicable

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Figures
OCT showed white thrombus after RA in calcified lesions. Case 1: Female, 64Y, coronary artery angiography shows proximal LAD 80% stenosis with severe calcification (1A). OCT shows maximum calcium angle 360°, maximum calcium thickness 1.34mm and minimal lumen area 1.17mm2 (1B). RA (1.5mm Burr, rotation speed 150,000rpm, ablation time 10s per RA, ablation number 4 times) was received before stent, OCT shows white thrombus after RA (1C, 1D).

Case 2: Male, 59Y, coronary artery angiography shows middle LAD 95% stenosis with severe calcification (2A). OCT catheter and 1.5mm balloon did not pass the lesion. So RA (1.5mm Burr rotation speed 156000rpm, ablation time 10s per RA, rotation number 5 times) was received, OCT shows maximum calcium angle 360°, maximum calcium thickness 1.12mm and minimal lumen area 1.34mm2, many white thrombus after RA (2B, 2C, 2D). 1.75 Burr was further used and implant stents finally.
Figure 2

OCT showed crack and dissection after RA in calcified lesions. OCT showed dissection (asterisks, A and C) and calcification crack (arrows, B and C)