Original

Significance of Coronary Artery Calcium Score in the Target Lesion Evaluated by Multi-detector Computed Tomography for Selecting Treatment of Rotational Atherectomy in Patients with Coronary Artery Disease

Teruo Sekimoto*[1], Yuji Hamazaki[1], Yasushi Akutsu[1, 2], Koshiro Sakai[1],
Ryota Kosaki[1] Hiroyuki Yokota[1], Tenjin Nishikura[1], Hiroaki Tsujita[1],
Seita Kondo[3], Satoshi Hosokawa[1], Shigeto Tsukamoto[1], Kyoichi Kaneko[1],
Mitsunori Muto[1], Masayuki Sakurai[3], Yusuke Kodama[1], Takehiko Sambe[2, 4],
Naoki Uchida[2, 4], Shinichi Kobayashi[2] and Youichi Kobayashi[1]

Abstract : We investigated whether coronary artery calcium score (CAC) in the target lesion on the multidetector computed tomography angiography (CTA) predicts the addition of the Rotational atherectomy (Rota) during percutaneous coronary intervention (PCI). Lesion CAC on CTA were evaluated with quantitative coronary analysis (QCA) on coronary angiography for predicting the Rota treatment in 114 consecutive patients (165 target lesions) with first PCI (68 ± 9 years old, females: 17.6%). Rota was added in 8 patients (11 lesions). The lesion length and diameter stenosis on QCA, and lesion length and lesion CAC on CTA were the primary factors associated with the addition of Rota. Using the cut-off value based on receiver operating characteristic analysis, the sensitivity and specificity for predicting the Rota based on QCA was 72.7% in 8 of 11 lesions (vessels) with Rota and the specificity was 74% in 114 of 154 without Rota in the lesion length of ≥ 23 mm ($\chi^2 = 10.9$, p = 0.001), and 54.5% in 6 of 11 lesions with Rota and the specificity was 79.2% in 122 of 154 without Rota in the diameter stenosis of ≥ 83% ($\chi^2 = 6.6$, p = 0.01). Those based on CTA were 90.9% in 10 of 11 lesions with Rota and 77.3% in 119 of 154 without Rota in the lesion length of ≥ 34 mm ($\chi^2 = 24.1$, p < 0.001), and 90.9% in 10 of 11 with Rota and 88.3% in 136 of 154 without Rota in the lesions with CAC ≥ 453 ($\chi^2 = 45.7$, p < 0.001). Lesion CAC on CTA is most predictive of addition of Rota during PCI.

Key words : coronary artery disease, rotational atherectomy, multidetector computed tomography angiography, calcification, quantitative coronary angiographic analysis.

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[1] *Division of Cardiology, Department of Medicine, Showa University School of Medicine*, 1-5-8 Hatanodai, Shinagawaku, Tokyo 142-8666, Japan.
[2] *Department of Internal Medicine (Cardiology), Clinical Research Institute for Clinical Pharmacology & Therapeutics, Showa University Karasuyama Hospital.*
[3] *Cardiovascular Center, Showa University Koto-Toyosu Hospital.*
[4] *Department of Clinical Pharmacology, Showa University School of Medicine.*
* To whom corresponding should be addressed.

Introduction

Calcified coronary lesions represent an advanced stage in the atherosclerotic process whereby a soft plaque is converted to a fibrocalcific plaque. The presence and severity of coronary artery lesion calcification impact the risk of subsequent coronary events and the success rate of percutaneous coronary intervention (PCI) in the obstructive coronary artery disease (CAD). Treatment of calcific lesions is challenging with higher rates of procedural failure, stent under-deployment, lower postprocedual minimal luminal diameter and acute gain, and an elevated risk of restenosis [1, 2]. Rotational atherectomy (Rota) has emerged to be a representative device for such calcified lesions. Rota can facilitate smooth stent delivery and stent expansion through lesion modification [3-5]. However, practice guidelines recommend the use of Rota for the treatment of heavily calcified or severely fibrotic lesions that cannot be bypassed by a balloon or adequately dilated before planned stenting during the PCI [6].

On the other hand, electron beam tomography is a noninvasive method to quantify the extent of calcium formation in the coronary arteries. Coronary artery calcium score (CAC) such as Agatston score [7] measured using multidetector computed tomography coronary angiography (CTA) can be used as an indicator of atherosclerotic burden [8].

In the present study, we retrospectively investigated whether quantitative calculating the CAC score in the target lesion by CTA could predict necessary of the use of Rota, before PCI in the CAD patients.

Subjects and methods

Populations

For this retrospective cohort study we used the information in consecutive 150 patients (208 target lesions) with CAD who was suspected by the CTA and underwent the percutaneous coronary intervention (PCI) within 6 months after the CTA from December 2010 to April 2014 at Showa university Hospital. The CAD was defined as the presence of at least one coronary lesion with ≥ 75% luminal diameter stenosis of coronary artery on CAG, and PCI was planned in our hospital. The patients with acute coronary syndrome or myocardial infarction who underwent the intervention or coronary artery bypass grafting in the past were excluded from the present study. Of those, 114 consecutive patients (165 target lesions) with first PCI (the mean ages ± standard deviations : 68 ± 9 years old, females : 17.6%) were finally selected in the present study. All patients gave written informed consent before the interventions, and the protocol was approved by our Institutional Review Board. Data collected retrospectively included : demographics, existing medical diagnoses, risk factors for cardiovascular disease, medications, previous cardiac procedures, and prior history of cardiac events.

QCA measurement on CAG and PCI with and without Rota

The coronary artery stenosis was assessed by quantitative coronary analysis (QCA) with CAAS software (Version 5.10, Pie Medical Imaging, Maastricht, Netherlands) [9]. The target

vessel, target lesion and lesion length (mm) on CAG were defined as the stenotic site of more than 75% using CAAS system. The minimum vascular diameter (mm), control vascular diameter (mm), and percent diameter stenosis (%) were also measured into target lesion.

All patients were fully informed about the alternative treatment options and PCI-related risks before they provided written informed consent to undergo the procedure. Furthermore, when the intravascular ultrasound (IVUS) catheter could not be passed through the severe lesions, when IVUS detected near-circumferential calcification, or when the lesion did not expand following balloon angioplasty, the final decision for Rota use was left to the discretion of the attending physician who was unaware of the calcified plaque conditions with CTA images. Rota was performed with the Rota system (Boston Scientific Corporation, Natick, MA, U.S.A.), with burr sizes from 1.25 to 2.25 mm. The recommended burr speed was 180,000–200,000 rpm with each sequence being less than 30 seconds, and care was taken to prevent any drop in rotational speed ≥ 5000 rpm. A continuous intracoronary infusion containing nicorandil, nitroglycerin and heparin was used to prevent and control slow-flow. It was advised to use incremental burr sizes to achieve a burr-to-artery ratio of at least 0.7. PCI was performed through the femoral artery approach by inserting a 7 Fr or 8 Fr guiding catheter under 10000 IU heparin intravenous administration by use of the approved systems (balloon length 10–40 mm). The technique to achieve an optimal angiographic result was determined by the operator. The procedural success was defined as angiographically proven residual stenosis less than 50 % and stenosis reduction of at least 20% [10]. The use of stents for bail out (flow-limiting dissections, severe recoil, vessel closure) or unsatisfactory results (residual diameter stenosis > 50%) was excluded from the present study.

CTA before CAG

CTA study was performed using a 128–slice scanner (Somatom Definition AS +; Siemens Medical Solutions, Forchheim, Germany) before CAG. The routine protocol for patients with suspected CAD included CAC measurement followed by noninvasive coronary angiography. Coronary calcium score was measured in a non–contrast-enhanced scan, quantified using the Calcium Score module of Syngo software (Siemens Medical Solutions) and expressed in Agatston units. Then, CTA studies were performed with a contrast-enhanced ECG gating, administering a β-blocker (a bolus injection of landiolol hydrochloride at a dose of 0.125 mg/kg) if the heart rate went above 70 beat/min. Nitroglycerine was administered sublingually immediately before the bolus injection of contrast media (Omnipaque, 350 mg iodine/ml, Daiichi Sankyo Co, Ltd, Tokyo, Japan) into the antecubital vein, followed by a 20 ml saline solution chaser bolus. The amount of the contrast media used for the scan was determined according to the patient's body weight and scan time [the total dose = (scan time + 4 seconds) × 0.07 × body weight]. The scan was gated to the cardiac cycle through ECG synchronization with the following parameters : collimation width, 64×0.6 mm ; rotation time, 330 ms ; tube voltage, 120 kV ; effective tube current, 800 mA ; table feed, 11.5 mm/rotation ; and pitch 0.3. ECG-gated data sets were finally reconstructed with a slice thickness of 2.0 mm at the point of the cardiac cycle for every 5% of R-R

interval.

Analysis of CTA and CAC measurements

Scans were analyzed off-line on a dedicated workstation (Leonardo, Siemens Medical Solution) to measure the CAC and the stenotic degrees of coronary artery. Each identified coronary artery lesion was assessed for stenosis severity along multiple longitudinal transverse, and oblique axes with the use of multiplanar reconstructions, thin-slab maximum intensity projections, and the curved reconstruction technique. The coronary lesion's severity was assessed by the maximum percent luminal diameter stenosis observed in any plane. The Agatston score, both per patient, per vessel, and target lesion [7, 11)] were measured for each patient. The lesion length including calcified plaque was measured on the longitudinal images. Two experienced observers, who were unaware of the patient's clinical information, evaluated the CTA images independently.

Calcified plaque patterns on CTA

Sharp reconstruction images were used for all plaque calcification analyses. Window width and level settings were adjusted to the investigator's discretion to optimally visualize the coronary artery lumen and to identify plaque calcification. Calcium plaque within CAD lesions were defined as occupying at least three contiguous pixels with a density of > 130 Hounsfield units (HU).

Statistical analysis

For descriptive purposes, the target lesions were divided into 2 groups on the basis of interventional treatment such as PCI with and without Rota. All continuous variables are presented as mean ± SD. Differences between groups were tested using an unpaired Student's test or χ^2 test. The associations between the predictors, such as calcium plaque pattern of the target lesion on CTA, were formally tested by multivariable logistic regression analysis for CT one-cross section of target lesion and one target lesion of coronary artery. All multivariable analyses employed the forward stepwise method, with entry and removal probability values set at 0.5. Pearson's correlation analysis was performed to assessment dependence. All statistical analysis was completed using IBM SPSS for Windows version 20 (SPSS Inc., an IBM Company, Chicago, IL). A probability value of < 0.05 was considered significant.

Results

A case with Rota

The CAG showed the coronary artery stenosis of $> 75\%$ in middle lesion of right coronary artery visually in 73-years-old woman (Fig. 1). QCA showed the following parameters of the 23.6 mm of length of target lesion, 2.98 mm of reference diameter, 0.72 mm of minimal lumen diameter, and 76 % of diameter stenosis. The catheter of IVUS did not pass through this target lesion, which indicated an extensively solid plaque with calcification. The treatment of Rota was achieved at bar size of 1.75 mm, and the coronary stenting with ballooning was achieved. The retrospective measurement of CAC on CTA was 2743.1 in the patient, 1698.1 in the target ves-
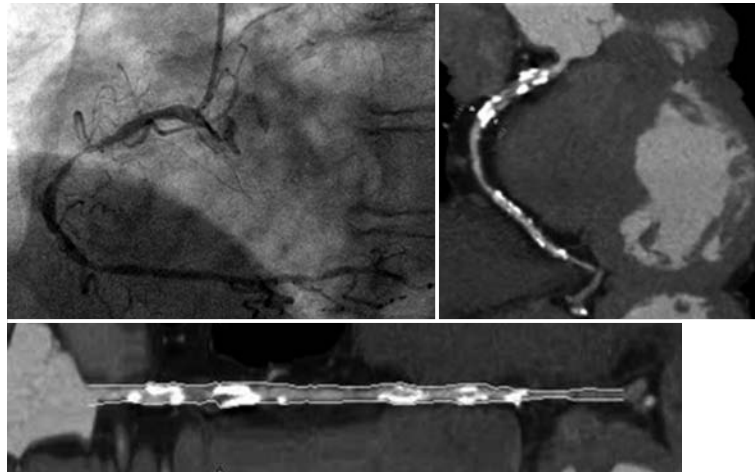
Fig. 1. The CAG showed the coronary artery stenosis of more than 75 % in the middle lesion of right coronary artery visually in 73 years old woman (Fig. 1). The catheter of IVUS did not pass through this target lesion, and the coronary artery ballooning failed despite of high pressure, which indicated extensively solid plaque with calcification. The treatment of Rota was achieved successfully, and the coronary stenting with ballooning was achieved. The lesion CAC on CTA showed high score.

sel, and 1034 in the target lesion. The length of calcified plaque on CTA was 39.9 mm on the longitudinal images.

Patients and lesion characteristics

In the present study, 106 patients underwent PCI without Rota and 8 patients with Rota, while in 4 patients the treatment as changed from PCI to Rota. Furthermore, 4 patients had PCI in one vessel and Rota in other vessel (These patients were evaluated as having the Rota). Among patient cohort, there was no significant difference in age, gender, risk factors, and medications between the patients with and without Rota (Table 1).

The PCI was involved in 5 vessels with LMT, 72 vessels with LAD, 37 vessels with LCX, and 51 vessels with RCA. There is no significant difference in the involved coronary artery area between the vessels with and without Rota (p = 0.71) (Table 2). Concerning every vessels, the target lesions with Rota were significantly longer lesion length (28.6 mm vs 20.5 mm, p < 0.01) and severe diameter stenosis (83.9% vs 78.1% , p = 0.05) on QCA, and higher CAC of target vessel and lesion (1078 vs 357 and 826 vs 176, p < 0.001 in each) and longer lesion length (45 mm vs 26.4 mm, p < 0.001) on CTA than those without Rota.

The factors for predicting the Rota

For continuous variables, the lesion length on QCA, and lesion length, and CAC in vessel and lesion on CTA were the primary factors associated with the Rota (Table 3). The lesion length was dependent on the diameter stenosis based on QCA with CAG (γ = 0.591, p < 0.001), and the lesion length on CTA was dependent on CAC in vessel and lesion based on CTA (γ = 0.514 and 0.537, p < 0.001 in each).

Table 1.　Patient characteristics

Variable	Rota		p value
	Yes　(n ＝ 8)	No　(n ＝ 106)	
Age（years）	73 ± 5	67 ± 10	p ＝ 0.07
Female	1（12.5%）	21（19.8%）	p ＝ 0.61
Diabetes	6（75%）	41（38.7%）	p ＝ 0.21
Hypertension	4（50%）	76（71.7%）	p ＝ 0.2
Hyperlipidemia	7（87.5%）	53（50%）	p ＝ 0.16
Current smoking	7（87.5%）	59（55.7%）	p ＝ 0.08
Familial history	2（25%）	16（15.1%）	p ＝ 0.41
History of hemodialysis	1（12.5%）	4（3.8%）	p ＝ 0.25
LVEF（%）	51.4 ± 23.2%	60.1 ± 15.5%	p ＝ 0.14
Medications before MDCT			
Use of beta blocker	1（12.5%）	7（6.6%）	p ＝ 0.53
Use of angiotensin-II receptor blocker	5（62.5%）	52（49.4%）	p ＝ 0.46
Use of statin	5（62.5%）	38（35.6%）	p ＝ 0.13
Use of aspirin	1（12.5%）	22（20.8%）	p ＝ 0.57

Abbreviations ; PCI ＝ Percutaneous coronary intervention, LVEF ＝ Left ventricular ejection fraction.

Table 2.　Vessel characteristics of CTA and CAG（QCA）

Variable	Rota		p value
	Yes　(n ＝ 11)	No　(n ＝ 154)	
Involved coronary artery	0 / 4（36.4%）/	5（3.2%）/ 68（44.2%）/	p ＝ 0.71
（LMT / LAD / LCX / RCA）	2（18.2%）/ 5（45.5%）	35（22.7%）/ 46（29.9%）	
QCA data of target lesion with CAG			
Lesion length（mm）	28.6 ± 8.1	20.5 ± 9.7	p ＝ 0.008
Reference diameter（mm）	3.01 ± 0.46	2.99 ± 0.63	p ＝ 0.92
Minimal lumen diameter（mm）	0.49 ± 0.25	0.66 ± 0.33	p ＝ 0.1
Quantitative diameter stenosis（%）	83.9 ± 0.09	78.1 ± 0.1	p ＝ 0.05
CTA data of target lesion			
Visual diameter stenosis	2（18.2%）/ 0 /	15（9.7）/10（6.5%）/	p ＝ 0.68
（100% / 99% / 90% / ＞ 90%）	6（54.5%）/ 3（27.3%）	92（59.7%）/ 37（24%）	
CAC data with CTA	51.4 ± 23.2%	60.1 ± 15.5%	p ＝ 0.14
in target vessel	1078 ± 516	357 ± 469	p ＜ 0.001
in target lesion（lesion CAC）	826 ± 324	176 ± 234	p ＜ 0.001
Lesion length（mm）	45 ± 12.3	26.4 ± 13.2	p ＜ 0.001

Abbreviations ; LMT ＝ Left Main Trunk, LAD ＝ Left Anterior Descending Coronary Artery, LCX ＝ Left Circumflex Coronary Artery, RCA ＝ Right Coronary Artery, QCA ＝ Quantitative Coronary Analysis on Coronary Angiography, CAG ＝ Coronary Angiography, CAC ＝ Coronary Artery Calcium score, CTA ＝ Multidetector Computed Tomography Angiography.

Table 3. Factors for predicting Rota selection in continuous valuables

Variable	Regression analysis Coefficient (beta)	Wald χ^2	Univariate analysis Odd ratio (95% CI)	p value
QCA data				
Lesion length (mm) (for increase)	0.064	6.22	1.07 (1.01–1.12)	p = 0.013
Diameter stenosis (%) (for increase)	0.054	3.53	1.06 (1–1.12)	p = 0.06
CTA data				
Lesion length (mm) (for increase)	0.068	13.42	1.07 (1.03–1.11)	p < 0.001
CAC in target vessel (for increase)	0.002	14.41	1.002 (1–1.003)	p < 0.001
CAC of target lesion (lesion CAC) (for increase)	0.005	19.96	1.005 (1.003–1.007)	p < 0.001

Abbreviations ; Rota = Rotational atherectomy, QCA = Quantitative coronary analysis on coronary angiography, CTA = Multidetector computed tomography angiography, CAC = Coronary artery calcium score.
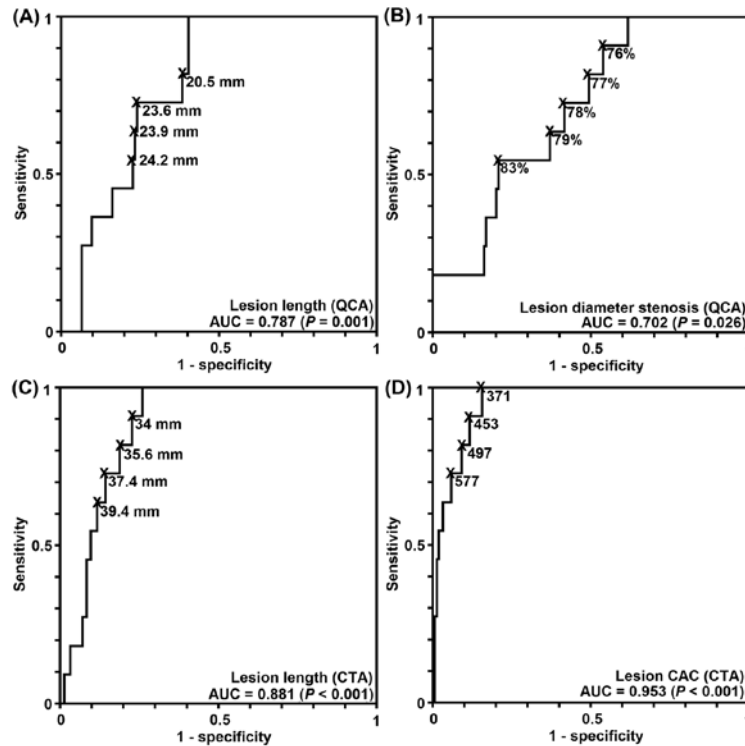

Fig. 2. Based on ROC analysis, the optimal thresholds for the Rota selection in vessel were at the lesion length of 23 mm (A) and stenosis diameter of 83% (B) on QCA, and at the lesion length of 34 mm (C) and lesion CAC of lesion of 453 (D). The sensitivity and specificity based on CTA were 90.9% in 10 of 11 lesions with Rota and 77.3% in 119 of 154 without Rota in the lesion length of ≥ 34 mm, and 90.9% in 10 of 11 with Rota and 88.3% in 136 of 154 without Rota in the lesion CAC ≥ 453 (χ^2 = 45.7, p < 0.001). The AUC for the prediction of Rota treatment was 0.953 in the lesion CAC on CTA, and it was the largest of the predictive factors.

Using the cut-off value based on ROC analysis (Fig. 2), the sensitivity and specificity for predicting the Rota based on QCA was 72.7% in 8 of 11 lesions (vessels) with Rota and the specificity was 74% in 114 of 154 without Rota in the lesion length of ≥ 23 mm, and 54.5% in 6 of 11 lesions with Rota and the specificity was 79.2% in 122 of 154 without Rota in the diameter stenosis of $\geq 83\%$. Similarly, the sensitivity and specificity based on CTA were 90.9% in 10 of 11 lesions with Rota and 77.3% in 119 of 154 without Rota in the lesion length of ≥ 34 mm, and 90.9% in 10 of 11with Rota and 88.3% in 136 of 154 without Rota in the lesion CAC ≥ 453 ($\chi^2 = 45.7$, $p < 0.001$). The area under ROC curve (AUC) in the lesion CAC for predicting the Rota was the largest in the predictive factors.

Discussion

In the present study, we showed that the target lesion CAC based on CTA was the most predictive of addition of the Rota during PCI.

Wang et al[12] demonstrated that a high CAC score (> 300) was a significant predictor for major adverse cardiac events (MACE) in patients with stable angina pectoris who underwent PCI, which indicated the complexity of PCI because of severely calcified plaque ; however, that study did not clarify the best tool for the decision of Rota use.

Practice guidelines recommend the use of Rota for the treatment of heavily calcified or severely fibrotic lesions that cannot be bypassed by a balloon or adequately dilated before planned stenting[13]. Despite the significant reduction of restenosis by Drug-eluting stent (DES), several factors including diabetes, hemodialysis, and severe calcification have been reported to be high-risk factors for restenosis after DES implantation[14-20]. Several studies have shown that DES implantation after the use of Rota reduced in the incident of target lesion revascularization (TLR)[21] and major adverse cardiac events[22-24]. It is that lesion modification by the Rota could yield smooth stent delivery, prevent damage to the polymer coating[25], and provide optimal stent expansion, all of which could help DES be effective, even for calcified lesions. In addition, procedural success rates of over 90 % and complications less than 5 % are routinely achieved after Rota of calcified lesions[26-28]. In the present study, no patient experienced emergency adverse events during PCI with the use of Rota such as a perforation of coronary artery and acute myocardial infarction, dissection of a coronary artery.

Development of CTA has elevated the non-invasive diagnosis of coronary heart disease to a new level. Particularly, in diagnosing calcification of coronary arteries, CTA has incomparable accuracy and allows quantification ; and the CAC score calculated using the automatic analysis software is favorably correlated, quantitatively, to the area of atherosclerotic plaques[7]. However, arterial wall calcification may adulterate the results of CTA, reducing the specificity and positive predictive value. Diederichsen et al[29] reported that the diagnostic accuracy of CTA declined in patients with high CAC (Agatston score > 400) and suggested that patients with CS > 400 should not undergo CTA. On the other hand, Lau et al[30] found that a high CAC improved the sensitivity of CTA in detecting a stenotic coronary artery, without compromising specificity. Furthermore, in cross-sectional images, Cerci R et al[31] reported that 79% of the plaques with $\geq$

180 calcium arc had $<$ 50% diameter of stenosis as defined by QCA and that 77% of lesions without visible residual lumen had 50% or greater lumen narrowing by QCA. It is important for the operator to predict the target lesions which are heavily calcified and undilatable with balloon technology before PCI[17] because the attempts to treat these heavily calcified lesions with ballooning and stenting often lead to vessel dissection or incomplete stent deployment with adverse outcomes. In the present study, we found that the target lesion CAC based on CTA was the most predictive of Rota addition during PCI with a sensitivity of 90.9% and the specificity of 88.3% in the lesion CAC ≥ 453 ($\chi^2 = 45.7$, p $<$ 0.001).

In conclusion, lesion CAC on CTA is most predictive of addition of Rota during PCI. The evaluation of CAC score on CTA is useful for indicating the addition of Rota.

The addition of Rota is recommended to be performed only when the heavily calcified lesion was not crossed by a balloon catheter or adequately dilated before stent implantation[6]. All the published prospective random control study that evaluated the various catheter-based coronary interventional devices excluded patients with severely calcified lesions[6]. Therefore, the evidence base for best PCI practices in patients with severely calcified lesions comes from nonrandomized single-arm studies although several retrospective studies have shown that the use of Rota before the attempt of stenting with ballooning is safe and reasonable in patients with severely calcified lesions. In the present study, the indication of Rota treatment was evaluated from CTA data retrospectively because of these reasons. Our results are based upon a single center experience with patients referred for CAD which may limit the more general application applicability of the findings. We also investigated the lesion calcified plaque on CTA as a predictor of Rota treatment in a limited number of patients. Thus, the evaluation of severely calcified plaque on CTA to decide the addition of Rota should be prospectively studied in the near future by a multicenter study.

Hemodialysis is generally known to cause the severe coronary artery calcifications, but only 5 patients with the history of hemodialysis was performed first PCI in the present study because the other patients with hemodialysis had been repeated PCI. Thus, the PCI procedure for those patients with hemodialysis should be also evaluated in future studies, independent of patients with only atherosclerosis.

Conflict of interest disclosure

The authors have declared no conflict of interest.

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