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Predictors of vessel quantitative flow ratio loss in patients with severely calcified lesions after rotational atherectomy

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Abstract

Background: *Previous studies have established that moderately to severely calcified lesions (MSCL) are associated with high rates of major adverse cardiovascular events, even when drug-eluting stents are implanted after rotational atherectomy (RA). Yet, the changes in coronary function indexes during follow-ups have never been investigated. The quantitative flow ratio (QFR), a novel coronary function index, has been increasingly adopted in daily practice in recent years.*

Methods: *A total of 111 MSCL patients were retrospectively enrolled in this study. The vessel QFR (QFRv) loss was defined as post-percutaneous coronary intervention QFRv minus follow-up QFRv. The study subjects were divided into high QFRv loss ($n = 51$) and low QFRv loss ($n = 60$) groups according to the binary method. The obtained predictors of QFRv loss were then analyzed.*

Results: *The results showed that the final burr-to-vessel ratio (B to V ratio) in the high QFRv loss group decreased significantly compared to the low QFRv loss group ($p < 0.01$). The univariate and multivariate regression analyses indicated that the final B to V ratio was an excellent predictor of QFRv loss. The cut-off value of the final B to V ratio for QFRv loss prediction was 0.50 (sensitivity: 50.98%, specificity: 68.33%, and area under the curve: 0.627 [95% confidence interval: 0.530–0.717], $p < 0.05$). Additionally, the target vessel failure incidence in the high QFRv loss group was higher than in the low QFRv loss group ($p < 0.01$).*

Conclusions: *An increased burr-to-vessel ratio can prevent QFRv loss in patients with MSCLs after RA, an effect that might be closely associated with a low target vessel failure incidence.* (Cardiol J 2023; 30, 3: 353–360)

Key words: percutaneous coronary intervention, rotational atherectomy, calcification, quantitative flow ratio

Introduction

Moderately to severely calcified lesions (MSCLs) in the coronary artery are usually a tricky lesion type during percutaneous coronary intervention (PCI). Accumulative data have shown that [1, 2] rotational atherectomy (RA) represents an effective method for MSCLs [3]. The concept of RA has been significantly improved from the original debulking to the current modifications,

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with greater emphasis on the creation of post-RA new surgical accesses for further balloon inflation and stent implantation [4].

The ROTAXUS trial revealed that, compared with stenting without RA, a routine CCL lesion preparation using RA before drug-eluting stent (DES) implantation did not decrease the primary 9-month endpoint of angiographic late lumen loss. However, the results also showed that the two studied groups had similar in-stent binary restenosis, target lesion revascularization, definite stent thrombosis, and major adverse cardiovascular events rates [5]. Subsequently, several follow-up studies were conducted on post-RA patients [5–8]. However, the changes in coronary physiological function indexes during follow-up have never been investigated because fractional flow reserve (FFR) measurement requires an invasive and complex procedure.

Recently, the quantitative flow ratio (QFR), a novel index for coronary physiological function assessment, has been increasingly adopted in daily practice as well as clinical trials [9–11]. QFR assessment is a high-quality angiographic image-based, noninvasive, and simple process that is easy to complete by computer analysis [9]. Additionally, it has been demonstrated that QFR is not significantly different from FFR and possesses an accuracy of 93.3% [9, 10]. Therefore, in this study, we retrospectively analyzed and compared the vessel QFR (QFRv) changes during PCI and follow-up time, aiming to find their predictive values for therapeutic optimization in patients with MSCL after RA.

Methods

Study population

A total of 279 patients with coronary artery calcification lesions, who underwent PCI after RA in Nanjing First Hospital, were retrospectively selected and enrolled in this study from January 2009 to September 2019. The inclusion criteria were as follows: (1) patients who met the indications for RA, (2) those who had coronaey angiography (CAG) images before PCI, immediately after PCI, and during the follow-up time, and (3) those who had high-quality CAG images with which the QFR value could be measured. The exclusion criteria were as follows: (1) incomplete CAG images, (2) no post-RA DES implant, (3) CAG images not adequate to measure the QFR value, (4) those with severe complications during RA (such as perforation and slow flow and no reflow after RA), (5) PCI history > 3 months, and (6) expected survival time < 12 months.

Vessel QFR loss was calculated (post-PCI QFRv — follow-up QFRv) and patients were divided into high QFRv (HQ) loss (QFRv loss > 0.01, n = 51) and low QFRv (LQ) loss (loss ≤ 0.01, n = 60) groups according to the median of QFRv loss (0.01).

Procedural protocol

To all patients 300 mg of clopidogrel (or 180 mg of ticagrelor), and a dose of intracoronary nitroglycerin were administered before the intervention. CAG was performed with 6-French catheters without a side hole using a conventional technique and a transradial approach. CAG images were obtained from multiple projections. A target vessel was defined as a coronary artery with MSCL-related myocardial ischemia. MSCL was graded based on CAG findings [12] or using intravascular ultrasound findings [13].

The technical aspects of the PCI procedure were determined by the practicing interventional doctor. The operation procedures and drugs used for PCI and RA were carried out according to the relevant guidelines and recommendations of the United States and Europe.

QFR computation

Offline QFR analysis was performed by a professional technician according to the previously described procedure and using AngioPlus QFR software (Pulse Medical Imaging Technology, Shanghai, China) (Fig. 1). The QFR was measured by two experienced researchers with a QFR reading license, and the number of measured cases was > 50. Additionally, its computation was performed offline in an independent laboratory according to the measurement procedures established by the FAVOR study [9]. The software automatically identified the morphology of the target vessel. Manual adjustments were made for low-resolution images, and the required QFR values were calculated through frame recording and with the contrast agent. The quantitative coronary angiography (QCA) data of each vessel were provided by software. The following QFR parameters were obtained for each target vessel: the lesion length, the minimal lumen diameter (MLD), the diameter stenosis (DS), the blood flow velocity, and the QFRv in selected vessels.

Study endpoints

The QFR of the entire target vessel was defined as QFRv, which was measured from the proxi-

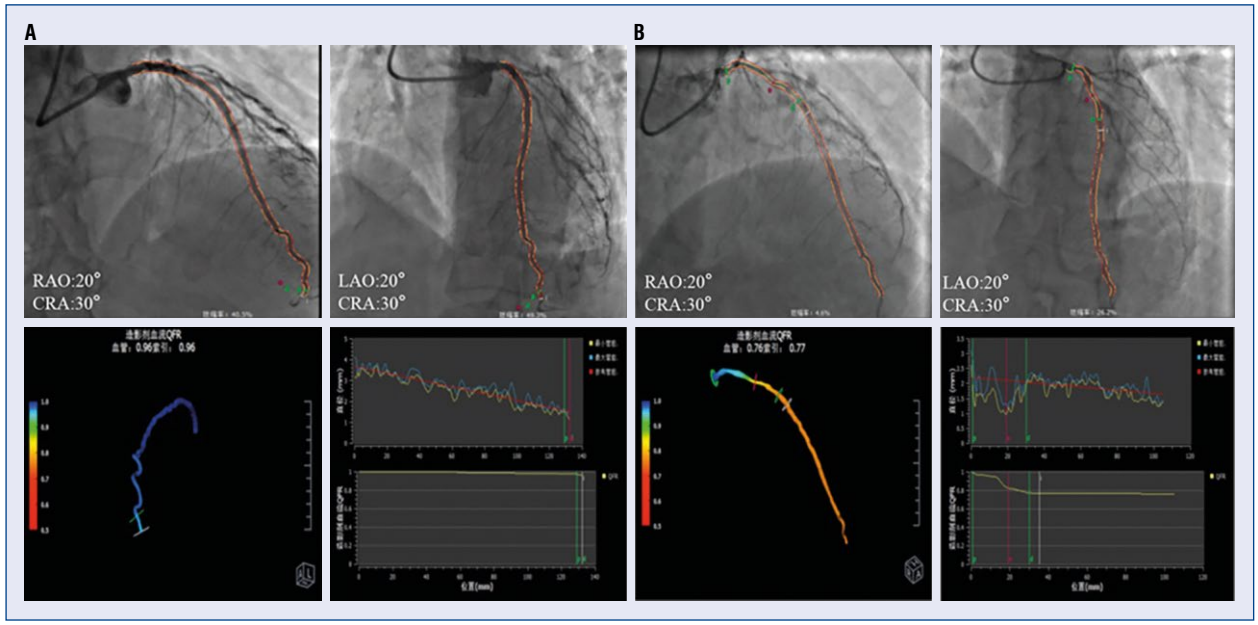

Figure 1. Vessel quantitative flow ratio (QFRv) loss analysis of a case; **A.** The post-percutaneous coronary intervention QFRv was calculated as 0.96; **B.** The follow-up QFRv was calculated as 0.77. QFRv loss in this case was 0.19 (0.96–0.77); CRA — cranial; LAO — left anterior oblique; RAO — right anterior oblique.

mal to the distal end of the vessel. The primary endpoint of this study was the analysis of the QFRv loss, expressed as the difference between the post-PCI QFRv and the follow-up QFRv. The secondary endpoint was the assessment of the target vessel failure (TVF), encompassing parameters such as cardiac death, target vessel myocardial infarction, and clinically driven target vessel revascularization [14]. The two reasons for the second CAG follow-up were as follows: (1) TVF driven and (2) CAG reexamination required by some of the patients. The period from the first CAG to the second was recorded as the follow-up time. Myocardial infarction was defined according to the European Society of Cardiology guideline [15].

Statistical analysis

Categorical variables were expressed in percentages and compared by the χ^2 test. Meanwhile, continuous variables were expressed as means with standard deviation or medians with quartile ranges and compared using the t-test (homogeneity of variance) or the rank sum test (heterogeneity of variance). Univariate and multivariate regression analysis were used to determine the predictive factors of QFRv loss. The receiver operating characteristic curve (ROC) was used to evaluate the variables' predictive ability of QFRv loss. SPSS 24.0 (SPSS Institute Inc.) software was used for all statistical analyses. The statistical significance was set at $p < 0.05$.

Results

Basic clinical data and TVF comparison between the LQ loss and the HQ loss groups for MSCL patients after RA

Finally, 111 patients, including 36 females and 75 males, were enrolled in this study, with an average age of 70.07 ± 7.36 years. The mean follow-up time of all patients was 382.8 ± 93.2 days. The incidence rates of diabetes, male gender, and TVF were significantly lower in the LQ loss group compared to the HQ loss group ($p < 0.01$ or $p < 0.05$). Additionally, the final burr-to-vessel ratio (B to V) of the LQ loss group was higher than that of the HQ loss group ($p < 0.01$) (Table 1). These results indicated that a higher QFRv loss was associated with male gender, diabetes, low final B to V, and high TVF in moderate to severe post-RA cases during the follow-up period.

QCA and QFRv data comparison between the LQ loss and the HQ loss groups in post-RA MSCL patients

The pre-PCI MLD and the MLD during the follow-up period, as well as the QFRv in the LQ loss group, were significantly higher compared to

Table 1. Basic clinical data and target vessel failure (TVF) between low QFRv (LQ) loss and high QFRv (HQ) loss groups in patients with moderately to severely calcified lesion after rotational atherectomy.

Variables	LQ loss group (Q loss ≤ 0.01, n = 60)	HQ loss group (Q loss > 0.01, n = 51)	P
Age [years]	70.18 ± 7.69	69.94 ± 7.02	0.864
Male	35 (58.33%)	40 (78.43%)	0.024
CV risk factors:			
Hyperlipidemia	38 (63.33%)	38 (74.51%)	0.207
Hypertension	42 (70.00%)	38 (74.51%)	0.598
Diabetes	17 (28.33%)	24 (47.06%)	0.042
Current smoker	23 (38.33%)	25 (49.02%)	0.257
Clinical diagnosis:			0.970
SAP	13 (21.67%)	9 (17.65%)	
UAP	38 (63.33%)	33 (64.71%)	
NSTEMI	5 (8.33%)	4 (7.84%)	
STEMI	4 (6.67%)	3 (5.88%)	
Medical treatment:			
Dual anti-platelet therapy	60 (100.00%)	51 (100.00%)	–
Statin therapy:			0.757
Atorvastatin	30 (50.00%)	27 (52.94%)	
Rosuvastatin	29 (48.33%)	21 (41.18%)	
Simvastatin	1 (1.67%)	3 (5.88%)	
ACEI/ARB	34 (56.67%)	26 (50.98%)	0.549
Disease vessel number:			0.824
Single-vessel disease	14 (23.33%)	11 (21.57%)	
Multi-vessel disease	46 (76.67%)	40 (78.43%)	
Lesion location:			1.000
LAD	49 (81.67%)	42 (82.35%)	
RCA	8 (13.33%)	7 (13.73%)	
LCX	3 (5.00%)	2 (3.92%)	
Initial burr size [mm]	1.43 ± 0.17	1.45 ± 0.19	0.539
Final burr size [mm]	1.53 ± 0.15	1.52 ± 0.21	0.782
Pre-PCI distal RVD [mm]	2.8 (2.5,3.4)	3.0 (2.4,3.2)	0.264
Final B to V	0.56 ± 0.05	0.53 ± 0.07	0.007
TVF	3 (5.00%)	21 (41.18%)	< 0.001

ACEI — angiotensin-converting enzyme inhibitors; ARB — angiotensin receptor antagonist; B to V — burr to vessel ratio; CV — cardiovascular; LAD — left anterior descending coronary artery; LCX — left circumflex coronary artery; NSTEMI — non-ST-segment elevation myocardial infarction; PCI — percutaneous coronary intervention; Q — QFRv; QFRv — vessel quantitative flow ratio; RCA — right coronary artery; RVD — reference vessel diameter; SAP — stable angina pectoris; STEMI — ST-segment elevation myocardial infarction; UAP — unstable angina pectoris

those of the HQ loss group ($p < 0.01$ or $p < 0.05$). Meanwhile, the DS of the LQ loss group was significantly lower than that of the HQ loss group during the follow-up period ($p < 0.01$) (Table 2). These results revealed that a lower MLD and a higher DS during the follow-up period could result in high QFRv loss in moderate to severe post-RA cases.

Regression and ROC analyses of QFRv loss predictors in patients with MSCL after RA

As shown by the univariate regression analysis, the final B to V represented an excellent predictor of QFRv loss in our post-RA patients ($p < 0.05$) (Table 3). The results of multivariate regression analysis showed that the final B to V was a better predictor of QFRv loss than the other

Table 2. Quantitative coronary angiography (QCA) vessel quantitative flow ratio (QFRv) and data between low QFRv (LQ) loss and high QFRv (HQ) loss groups in patients with moderately to severely calcified lesions after rotational atherectomy.

Variables	LQ loss group (Q loss ≤ 0.01, n = 60)	HQ loss group (Q loss > 0.01, n = 51)	P
Pre-PCI:			
Lesion length [mm]	58.50 (40.95, 71.90)	64.90 (49.20, 77.80)	0.064
MLD [mm]	1.1 (0.9, 1.2)	0.9 (0.8, 1.0)	0.031
DS [%]	58.4 (52.0, 65.8)	60.2 (53.3, 64.5)	0.962
FV [m/s]	0.14 (0.09, 0.17)	0.15 (0.10, 0.17)	0.320
QFRv	0.56 (0.41, 0.68)	0.57 (0.41, 0.68)	0.711
Post-PCI:			
Total stent length [mm]	60.00 (46.00, 76.50)	66.00 (51.00, 79.00)	0.252
Stent number	2.0 (2.0, 3.0)	2.0 (2.0, 3.0)	0.149
MLD [mm]	2.1 (1.8, 2.4)	2.1 (1.7, 2.4)	0.279
DS [%]	23.6 (18.5, 29.9)	25.3 (21.9, 32.8)	0.140
FV [m/s]	0.20 (0.14, 0.25)	0.21 (0.16, 0.27)	0.454
QFRv	0.93 (0.89, 0.96)	0.92 (0.90, 0.98)	0.260
Follow-up:			
MLD [mm]	2.1 (1.7, 2.2)	1.6 (1.1, 2.3)	0.002
DS [%]	26.90 (22.03, 32.03)	33.20 (24.50, 57.50)	< 0.001
FV [m/s]	0.14 (0.12, 0.19)	0.15 (0.11, 0.20)	0.932
QFRv	0.95 (0.92, 0.98)	0.83 (0.72, 0.93)	< 0.001

DS — diameter stenosis; FV — flow velocity; MLD — minimal luminal diameter; PCI — percutaneous coronary intervention

Table 3. Predictors of vessel quantitative flow ratio (QFRv) loss analyzed by univariate and multivariate regression in patients with moderately to severely calcified lesions after rotational atherectomy.

Variables	Univariate regression OR (95% CI)	P	Multivariate regression OR (95% CI)	P
Age [years]	1.004 (0.943–1.070)	0.890		
Male [%]	0.682 (0.244–1.911)	0.682		
Diabetes [%]	0.707 (0.278–1.798)	0.467		
Multi-vessel disease	0.672 (0.205–2.196)	0.510		
Total stent length [mm]	1.018 (0.996–1.039)	0.104		
Lesion length [mm]	1.011 (0.991–1.031)	0.533		
Pre-PCI MLD [mm]	0.181 (0.029–1.119)	0.066		
Pre-PCI DS [%]	1.020 (0.975–1.066)	0.623		
Pre-PCI QFRv	0.193 (0.016–2.331)	0.195		
Final B to V	0.852 (0.779–0.933)	0.001	0.858 (0.781–0.943)	0.001
Post-PCI MLD [mm]	0.412 (0.140–1.213)	0.107		
Post-PCI DS [%]	1.067 (1.005–1.133)	0.033	0.998 (0.996–1.001)	0.147

B to V — bur-to-vessel ratio; CI — confidence interval; DS — diameter stenosis; MLD — minimal lumen diameter; OR — odds ratio; PCI — percutaneous coronary intervention

assessed factor (post-PCI DS) ($p < 0.01$) (Table 3). The ROC analysis at the follow-up time also showed that the cutoff value of the final B to V was 0.50, with a sensitivity of 50.98%, a specificity of 68.33%, a Youden index of 0.193, and an area under the curve (AUC) of 0.627 (95% confidence interval [CI]: 0.530–0.717) ($p < 0.05$ or $p < 0.01$) (Fig. 2). These results showed that an increased final B

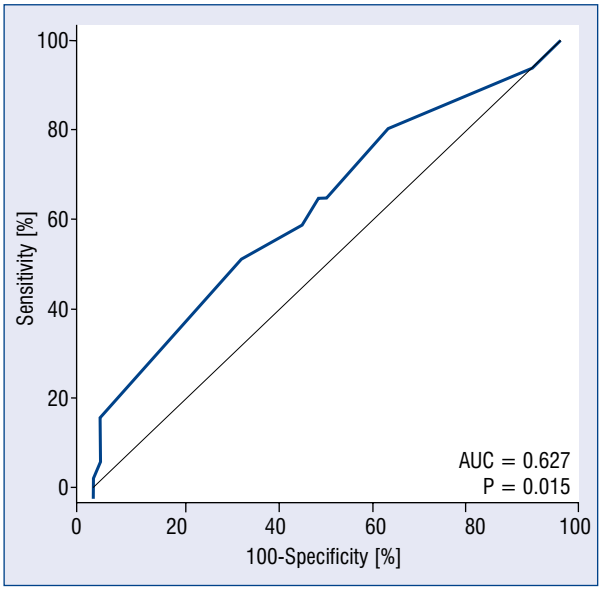

Figure 2. Receiver operating characteristic curve data of burr-to-vessel ratio (B to V) for predicting vessel quantitative flow ratio loss in patients with moderately to severely calcified lesions after rotational atherectomy; AUC — area under the curve.

to V could reduce QFRv loss in patients with MSCL after RA at the follow-up time.

Discussion

This study explored, for the first time, the possibility of utilizing QFRv loss as a viable parameter reflecting coronary physiological function in post-RA MSCL patients. Indeed, the loss of post-follow-up coronary physiological function has never been studied before, mainly because FFR determination requires an expensive pressure wire, and the measuring process is complex, which makes it difficult for researchers to quantify the data changes related to coronary physiological function during follow-up [16]. Previous studies have shown that FFR measured immediately after PCI in patients without RA was lower than a certain value that correlated with the occurrence of clinical adverse events [17–20]. It became easier to conduct coronary physiological function measurements during the follow-up period with the emergence of non-invasive and simple QFR determination methods [9]. In the present study, we found that an increased burr-to-vessel ratio could decrease QFRv loss in MSCL patients after RA during the follow-up, which might be closely associated with low TVF incidence. It is worth noticing that this is the first mention of such findings.

The upfront RA before contemporary DES in severe calcified lesion cases is feasible in modern PCI, and it is associated with a higher success rate [21]. A randomized trial comparing small (burr-to-vessel ratio of ≤ 0.7) and large (burr-to-vessel ratio of > 0.7) burrs revealed that the smaller ones achieved similar immediate lumen enlargement and late target vessel revascularization as the larger burrs, with fewer complications [22]. The European expert consensus document recommends a burr-to-vessel ratio of 0.6, while the North American expert consensus document recommends a burr-to-vessel ratio of 0.4–0.6 [23, 24]. Unfortunately, there are no current data on the relation between burr-to-vessel ratio and coronary physiological functions. The present study found that increasing the burr-to-vessel ratio (≥ 0.50) could reduce QFRv loss during the follow-up period.

Current accumulative data have shown a significant association between post-PCI without RA low FFR value and a higher clinical adverse event risk at mid- and long-term follow-ups [19, 20, 25]. Our study also reflected that the incidence rate of TVF in the LQ loss group was significantly lower compared to the HQ loss group, indicating that a lower QFRv loss might be closely associated with a lower TVF incidence. Additionally, Nozue et al. [26] reported that DS was significantly determinant for coronary computed tomography angiography-derived fractional flow reserve (FFRCT). Moreover, Chen et al. [27] revealed, after adjusting, through QRF, the low-density lipoprotein cholesterol goal for coronary physiology, that the goal-achievement group exhibited lower DS with a better change in QFR and a lower incidence of major adverse cardiovascular events at 1-year follow-up [27]. Interestingly, our study's DS follow-up was also lower in the LQ loss patients compared to their HQ loss counterparts. In summary, these findings indicated that there might be a close correlation between angiographic stenosis and coronary physiological functions.

Limitations of the study

This study's shortcomings are as follows: (1) its retrospective (not prospective) nature — fewer than 50% of patients had a follow CAG; (2) the sample size was relatively small; and (3) the potential impacts of long-term inclusion-related variations in treatment strategies and guideline changes on the outcomes.

Conclusions

In conclusion, high burr-to-vessel ratio (≥ 0.50) had a high predictive value for low QFRv loss in patients with MSCL after RA, which may be closely associated with low occurrence of TVF. It implies that the benefit of increased burr size is reflected in reduced coronary physiological dysfunction and TVF occurrence in these patients.

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Conflict of interest: None declared

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