Post-PCI quantitative flow ratio predicts 3-year outcome after rotational atherectomy in patients with heavily calcified lesions

Wei You MD | Yuhe Zhou MD | Zhiming Wu MD | Peina Meng MD | Defeng Pan MD | Delu Yin MD | Song Yang MD | Xiangqi Wu MD | Fei Ye MD

1Division of Cardiology, Nanjing First Hospital, Nanjing Medical University, Nanjing, China
2Division of Cardiology, The First Affiliated Hospital of Anhui Medical University, Hefei, China
3Division of Cardiology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, China
4Division of Cardiology, The First People’s Hospital of Lianyungang, Lianyungang, China
5Division of Cardiology, Yixing People’s Hospital, Yixing, China

Correspondence
Fei Ye, Department of Cardiology, Nanjing First Hospital, Nanjing Medical University, 68 Changle Rd, 210006 Nanjing, China.
Email: njsdxxn2017@163.com
Xiangqi Wu, Division of Cardiology, Nanjing First Hospital, Nanjing Medical University, Nanjing, China.
Email: wuxq2018@tom.com

Funding information
Nanjing Municipal Science and Technology Bureau, Grant/Award Number: 201803008; Cardiocare Sponsored (CS) Optimized Antithrombotic Research Fund, Grant/Award Number: BJUHFCOARF201801-13

Abstract

**Background:** The study sought to investigate the clinical predictive value of quantitative flow ratio (QFR) for the long-term outcome in patients with heavily calcified lesions who underwent percutaneous coronary intervention (PCI) following rotational atherectomy (RA).

**Methods:** In this retrospective study, 393 consecutive patients from 2009 to 2017 were enrolled. The QFR of the entire target vessel (QFRv) and the QFR of the stent plus 5 mm proximally and distally (in-segment) (QFRi) were measured. The primary endpoint was target lesion failure (TLF), including target lesion-cardiac death (TL-CD), target lesion-myocardial infarction (TL-MI), and clinically driven-target lesion revascularization (CD-TLR).

**Results:** A total of 224 patients with 224 calcified lesions completed the clinical follow-up, and 52 patients had TLF. There was no significant difference in QFRv post-PCI between non-TLF and TLF groups (p > .05). However, QFRi post-PCI was significantly higher in the non-TLF group than in the TLF group. Multivariate Cox regression showed that QFRi post-PCI was an excellent predictor of TLF after a 3-year follow-up (HR 1.7E−8 [5.3E−11–5.6E−6]; p < .01). Furthermore, receiver-operating characteristic curve analysis demonstrated that the optimal cutoff value of QFRi for predicting the long-term TLF was 0.94 (area under the curve: 0.826, 95% confidence interval: 0.756–0.895; sensitivity: 89.5%, specificity: 69.2%; p < .01). The QFRi ≤ 0.94 post-PCI was negatively associated with TLF, including TL-CD, TL-MI, and CD-TLR (p < .01).

**Conclusions:** QFRi post-PCI showed a high predictive value for TLF for during a 3-year follow-up in patients who underwent PCI following RA; specifically, lower QFRi values post-PCI were associated with worse TLF.

**Keywords**
calcified lesion, patients, percutaneous coronary intervention, quantitative flow ratio, rotational atherectomy
1 | INTRODUCTION

Rotational atherectomy (RA) technique was first introduced more than 30 years ago and used to reduce plaque burden by the debulking idea before the stent era and by the modification idea in the current stage. However, both strategies failed to be proven superior to only balloon angioplasty, bare-metal stent (BMS) implantation, or drug-eluting stent (DES) implantation for coronary calcified lesions in a number of previous studies. At present, the significant indications of RA in daily practice are limited to heavily calcified lesions detected by coronary angiography (CAG) or intravascular imaging (IVI) as a bailout strategy. A previous study has shown that the final minimal luminal diameter (MLD) post-BMS implantation following RA was the only significant independent predictor of event-free survival. Even with DES used in the current stage for complex coronary lesions with/without the use of RA, nearly one-third of patients experienced major adverse cardiac events (MACE, defined as the composite of death, myocardial infarction, and target vessel revascularization [TVR]) at 2-year follow-up. A question arises as to why percutaneous coronary intervention (PCI) of heavily calcified lesions can cause poor outcomes, we hypothesize that not only because of RA itself (which can cause thermal injury and additional vessel trauma and decrease the efficacy of DES in reducing neointimal growth) but unsatisfactory lesion preparation could also influence the final stent result. A physiological index such as fractional flow reserve (FFR) post-PCI without RA has a good predictive value for the late outcome of target vessel failure (TVF, defined as the composite of cardiac death, target vessel-related myocardial infarction, and clinically driven TVR). However, previous studies have not focused on the predictive value of physiological indexes post-PCI on clinical outcome after the PCI procedure using RA due to complex manipulation of pressure wire.

Quantitative flow ratio (QFR), a novel physiological index derived from three-dimensional (3-D) angiographic analysis positively correlates with traditional invasive FFR, as shown in many studies. The main advantage is that QFR measurement does not require hyperemia and a pressure wire. The online or offline analysis permits physiological guiding of PCI and retrospective physiological functional studies if the angiographic quality is satisfied. Therefore, we designed a retrospective study to determine the predictive value of QFR post-PCI for the target lesion failure (TLF) in the long-term follow-up. Currently, the QFR research has mainly focused on the vessel QFR, and there have been no studies on the stent QFR. Generally, the definition of the stent segment includes the stent segment and the 5-mm area from its proximal and distal ends. In this study, we aimed to compare the predictive value of TLF between the vessel QFR and the stent QFR post-PCI in patients with heavily calcified lesions using the RA technique.

2 | MATERIALS AND METHODS

2.1 | Study design

This was a retrospective cohort study. The study protocol was approved by the ethics committees of the four participating centers (Nanjing First Hospital, the Affiliated Hospital of Xuzhou Medical University, the First People's Hospital of Lianyungang, and Yixing People's Hospital), and the study was performed in accordance with the Declaration of Helsinki. All of the patients had signed informed consent twice during the in-hospital period, that is, first, they signed informed consent for the RA procedure, and second, they signed informed consent for the clinical follow-up in the retrospective study for the second time.

A total of 393 consecutive patients who had undergone RA management during the elective PCI for de novo calcified lesions in four hospitals from January 2009 to May 2017 were enrolled in this study. All clinical and PCI procedure variables were recorded from the follow-up groups of the four hospitals (Nanjing First Hospital, the Affiliated Hospital of Xuzhou Medical University, the First People's Hospital of Lianyungang, and Yixing People's Hospital). Two experienced technicians blinded to follow-up results independently measured clinical records and angiographic and QFR data. The study flowchart is shown in Figure 1.

2.2 | Study population

We included patients treated with RA for target lesions with the indications of heavily calcified lesions (detected by angiography or IVI), or uncrossable or undilated calcified lesions. The exclusion criteria were as follows: severe complications of RA, such as perforation, post-PCI slow flow or no flow (defined as coronary thrombolysis in myocardial infarction flow grade <3 or =0); culprit lesions that were not de novo lesions, such as in-stent restenosis (ISR); PCI with drug-coated balloon(s) or bioabsorbable scaffold implantation post-RA; previous target vessel PCI; and a life expectancy < 12 months.

2.3 | PCI procedure

All of the patients were administered 300 mg clopidogrel as a loading dose before CAG. Unfractionated heparin (100–120 μg/kg) was administered by bolus injection via sheath to maintain activated clotting time (ACT) > 300 s during the whole procedure. Standard selective CAG was performed via a radial approach with 6-French catheters without a side hole in accordance with the routine practice. Intracoronary nitroglycerin (200 μg) was injected before selective CAG.

RA was performed using a Rotablator (Boston Scientific). The initial and final burr size with a floppy RotaWire (Boston Scientific) was at operator’s discretion. The initial burr speed ranged from 135 000/min to 180 000/min, and the RA solution was a cocktail of verapamil, nitroglycerine, and heparin. Moreover, 98.7% of the procedures (221 of 224 patients) were performed with the radial approach, and in 94.2% of the patients (211 of 224 patients), guiding catheters were up to 6F in diameter. IVI was used for the PCI guidance in only 54.5% of the patients (122 of 224 patients). After the culprit vessel had been solved...
Patients’ clinical, demographic data, cardiovascular risk factors, medical treatment, and clinical follow-up data were collected from the follow-up group in the above four hospitals. Clinical follow-up was performed for all 224 patients, and CAG follow-up was conducted in 112 patients. The CAG procedure was performed 1 year after PCI. The median clinical follow-up duration was 1095 days (interquartile range [IQR]: 1095–1095 days).

The primary endpoint was TLF at the 3-year clinical follow-up. TLF was defined as a composite of target lesion-related cardiac death (TL-CD), target lesion-related myocardial infarction (TL-MI), and clinically driven-target lesion revascularization (CD-TLR) by coronary artery bypass graft surgery (CABG) or PCI. TL-CD was defined as all-cause death unless an unequivocal noncardiac cause or nontarget lesion-related cause was established. The definition of MI was in accordance with the guidelines of the European Society of Cardiology (ESC). TL-MI occurrence without an identified culprit vessel was considered as a target lesion-related. CD-TLR was defined as any repeated revascularization in the presence of a lesion with percent-diameter stenosis (%DS) > 90%, or %DS > 50% accompanied with relevant evidence of angina plus objective signs of ischemia at rest or during exercise, or relevant positive ischemic evidence on any noninvasive functional stress test. All of the events were judged by an independent clinical event committee that was blinded to the PCI procedure and QFR and QCA data.

2.7 | Statistical analysis

According to the ROTAXUS trial, the MACE rate was 29.4% in patients with heavily calcified lesions after the RA procedure at a 2-year follow-up. The predictor had a standard deviation of 0.05, and the hazard ratio (HR) was set at 1.0. We tested the hypothesis using a 5% significance level with a two-sided Wald test. As a result, the sample size of 224 was calculated with 1.00 power by PASS11.0 software (NCSS, LLC).

Categorical variables were expressed as counts with percentages, whereas continuous variables were expressed as mean with standard deviation (SD) or median with IQRs. Categorical variables were compared using the $\chi^2$ test. The Kolmogorov–Smirnov test was used to assess the distributions of continuous variables. Continuous variables were expressed as mean $\pm$ SD for normally distributed data.
and were compared using the Student’s t test. Data that were not normally distributed were expressed as medians and were compared using the Mann–Whitney U test. The Kaplan–Meier method was used to derive the event rates at the follow-up and to plot time-to-event curves, which were then compared by the log-rank test. To study TLF predictors, a univariate Cox regression was performed. Variables that were found to be significant were entered into a multivariate model. Their outputs included HR, 95% confidence interval (CI), and p value. The receiver operating characteristic curve was used to compare the variables’ predictive ability of the rates of TLF. All of the statistical tests were two-tailed. Statistical significance was set at .05. For the statistical analysis, the SPSS version 24.0 (SPSS Institute Inc.) was used.

3  |  RESULTS

3.1  |  Basic clinic, procedural, and QCA data of patients with heavily calcified lesions with and without TLF after RA

A total of 71.8% of the patients (282/393) finished clinical follow-up at 3 years if they had no symptoms, or at least 3 years if they felt chest pain during exercise or had other clinical ischemic evidence or acute coronary syndrome (ACS). Among them, 47 cases had a low-quality CAG, which did not satisfy the criterion for QFR measurement; six patients were treated with a drug-coated balloon without DES implantation; two patients had perforation as a complication; and three patients had severely slow or no flow post-RA combined with periprocedural MI. Finally, 224 patients were eligible for inclusion in the current study. Among 172 patients with multivessel disease, 170 underwent complete revascularization.

No significant differences between TLF and non-TLF groups were detected in age, gender, family history of coronary artery disease (CAD), cardiovascular risk factors (hyperlipidemia, hypertension, diabetes, current smoker, renal insufficiency, and hemodialysis), clinical diagnosis (stable angina pectoris [SAP], unstable angina pectoris [UAP], non-ST-segment elevation myocardial infarction [NSTEMI], and ST-segment elevation myocardial infarction [STEMI]), antiplatelet therapy, statin therapy, single-vessel disease, multivessel disease, pre-PCI proximal and distal RVDs, pre-PCI DS, lesion length, pre-dilated balloon diameter, pre-dilated pressure, post-dilated balloon diameter, post-PCI proximal and distal RVDs, total stent length, average stent diameter, stent number, QFRv post-PCI, burr to vessel diameter ratio, imaging use, cutting balloon (CB) use, and blood flow velocity (FV) post-PCI (p > .05) (Table 1). However, the target vessel location in the TLF group was significantly different from that in the non-TLF group (p < .05). Post-dilated pressure and post-PCI DS of the TLF group were notably higher than those in the non-TLF group, and post-PCI MLD and QFRI post-PCI of the TLF group were markedly lower (p < .05 or p < .01) (Table 1).

| Variable | TLF (N = 52) | Non-TLF (N = 172) | p value |
|----------|--------------|------------------|---------|
| Age, years | 71.5 ± 8.0 | 71.0 ± 7.6 | .690 |
| Male (%) | 33 (63.5%) | 119 (69.2%) | .439 |
| Family history of CAD (%) | 2 (3.8%) | 5 (2.9%) | .665 |
| CV risk factors | | | |
| Hyperlipidemia (%) | 38 (73.1%) | 117 (68.0%) | .489 |
| Hypertension (%) | 36 (69.2%) | 132 (76.7%) | .273 |
| Diabetes (%) | 23 (44.2%) | 68 (39.5%) | .546 |
| Current smoker (%) | 21 (40.4%) | 70 (40.7%) | .968 |
| Renal insufficiency (%) | 5 (9.6%) | 9 (5.2%) | .323 |
| Hemodialysis (%) | 2 (3.8%) | 4 (2.3%) | .625 |
| Clinical diagnosis | | | .512 |
| SAP (%) | 11 (21.2%) | 29 (16.9%) |
| UAP (%) | 27 (51.9%) | 105 (61.0%) |
| NSTEMI (%) | 5 (9.6%) | 19 (11.0%) |
| STEMI (%) | 9 (17.3%) | 19 (11.0%) |
| Antiplatelet therapy | | | |
| Aspirin (%) | 52 (100%) | 172 (100%) | – |
| Clopidogrel/Ticagrelor (%) | 52 (100%) | 172 (100%) | – |
| Clopidogrel (%) | 32 (61.5%) | 113 (65.7%) | .582 |
| Statin therapy (%) | | | .128 |
| Atorvastatin | 30 (57.7%) | 88 (51.2%) |
| Rosuvastatin | 20 (38.5%) | 77 (44.8%) |
| Simvastatin | 0 (0%) | 6 (3.5%) |
| QCA data | | | .250 |
| Vessel disease number | | | |
| Single vessel disease (%) | 9 (17.3%) | 43 (25.0%) |
| Multiple vessel disease (%) | 43 (82.7%) | 129 (75.0%) |
| Target vessels | | | .020 |
| LAD (%) | 34 (65.4%) | 143 (83.1%) |
| RCA (%) | 14 (26.9%) | 21 (12.2%) |
| LCX (%) | 4 (7.7%) | 8 (4.7%) |
| Pre-PCI distal RVD (mm) | 2.4 (2.1,2.6) | 2.3 (2.0,2.7) | .228 |
| Pre-PCI proximal RVD (mm) | 2.8 (2.3,3.2) | 2.8 (2.4,3.2) | .465 |

(Continues)
Furthermore, we analyzed the minimal stent diameter, maximal stent diameter, minimal stent area, and stent eccentricity index in patients with heavily calcified lesions immediately after PCI. The minimal stent diameter, minimal stent area, and stent eccentricity index in the non-TLF group were larger than those in the TLF group ($p < .05$). However, there was no significant difference in maximal stent diameter between the two groups ($p > .05$) (Table 51). At 1-year follow-up, there were no differences in proximal RVD and distal RVD between the TLF group and the non-TLF group ($p > .05$). However, MLD in the TLF group was smaller than that in the non-TLF group, and DS in the TLF group was larger ($p < .05$) (Table 52).

These results indicated that TLF occurrence was closely related to post-dilated pressure, MLD, DS, and QFRi post-PCI, and MLD and DS 1 year after PCI in patients with heavily calcified lesions after RA. Moreover, lower minimal lumen diameter, minimal stent area, and eccentricity index were associated with a failure rate of the target lesion.

### 3.2 Cox regression analysis of factors associated with TLF and their predictive value analyzed by ROC curve in patients with heavily calcified lesions after RA at 3-year follow-up

To further analyze factors associated with TLF in patients with heavily calcified lesions after RA at 3-year follow-up, we used the univariate and multivariate Cox regression methods. As shown by the univariate Cox regression analysis, post-dilated pressure, MLD, DS, QFRv, and QFRi post-PCI, as well target vessel LAD, were able to predict TLF in these patients after RA ($p < .05$ or $p < .01$) (Table 2). Next, these six factors were used in the multivariate Cox regression analysis. DS and QFRi post-PCI, and target vessel LAD were better predictors of TLF than the other three factors (postdilated pressure, and MLD and QFRv post-PCI) in these patients ($p < .01$) (Table 2). The ROC analysis showed that the cutoff value of QFRi post-PCI was 0.94, with a sensitivity of 89.50%, specificity of 69.20%, Youden index of 0.587, and area under the curve (AUC) of 0.826 (95% CI: 0.756–0.895) for predicting TLF at the 3-year follow-up ($p < .01$) (Figure 2).

These results suggested that QFRi post-PCI was an excellent predictor of TLF in patients with heavily calcified lesions after RA at the 3-year follow-up.

### 3.3 Clinical outcome in patients with heavily calcified lesions after RA at the 3-year follow-up

According to the QFRi post-PCI cutoff value of 0.94, we divided these patients into high- and low-QFR groups. The incidence rate of TLF, TL-CD, TL-MI, and TLR in the high-QFR group were significantly lower than those in the low-QFR group ($p < .05$ or $p < .01$) (Table 3). TLF and its compositions analyzed using the Kaplan–Meier curves are shown in Figure 3. The TLF ratio in the low-QFRi group was significantly higher than in the high-QFRi group (66.7% vs. 9.4%, $p < .0001$, HR: 10.35 [95% CI: 5.09–21.04]). Further analysis showed...
that TL-CD (11.1% vs. 3.5%, \( p = .003 \), HR: 8.46 [95% CI: 1.11–64.66]), TL-MI (20.4% vs. 2.9%, \( p < .0001 \), HR: 9.42 [95% CI: 2.70–32.90]), and TL-TLR (55.6% vs. 5.9%, \( p < .0001 \), HR: 15.57 [95% CI: 6.96–34.81]) were higher in the low-QFRi group than in the high-QFRi group.

These results revealed that the cutoff value (0.94) after QFRi post-PCI could differentiate the risk level of TLF occurrence in patients with heavily calcified lesions after RA at the 3-year follow-up.

### DISCUSSION

For the first time, we investigated the low QFRi post-PCI (\( \leq 0.94 \)) in patients who underwent RA and the second-generation DES implantation showed a substantial predictive value of high TLF at the 3-year follow-up. The analysis of QFR computation post-PCI for evaluating lesion burden of the residual physiological vascular is more convenient than the traditional FFR measurement. Previous studies

### TABLE 2  Predictors of TLF were analyzed by the Cox regression method

| Variables                                | Univariate analysis HR (95% CI) | \( p \) Value | Multivariate analyses HR (95% CI) | \( p \) Value |
|-------------------------------------------|---------------------------------|--------------|----------------------------------|--------------|
| Male (%)                                  | 1.246 (0.708–2.191)             | .445         |                                  |              |
| Age (years)                               | 1.007 (0.972–1.044)             | .696         |                                  |              |
| Hypertension (%)                          | 0.738 (0.409–1.329)             | .311         |                                  |              |
| Hyperlipidemia (%)                        | 1.236 (0.670–2.282)             | .498         |                                  |              |
| Diabetes (%)                              | 1.184 (0.685–2.046)             | .546         |                                  |              |
| Smoking (%)                               | 0.984 (0.566–1.713)             | .956         |                                  |              |
| Single-vascular lesion (%)                | 0.643 (0.313–1.318)             | .228         |                                  |              |
| Multiple-vascular lesion (%)              | 1.556 (0.758–3.192)             | .228         |                                  |              |
| Target-lesion length (mm)                 | 1.001 (0.989–1.013)             | .915         |                                  |              |
| pre-PCI DS (%)                            | 0.989 (0.961–1.018)             | .464         |                                  |              |
| Initial burr size (mm)                    | 0.539 (0.112–2.600)             | .441         |                                  |              |
| Final burr size (mm)                      | 0.548 (0.120–2.497)             | .437         |                                  |              |
| Pre-dilated balloon diameter (mm)         | 0.779 (0.384–1.581)             | .490         |                                  |              |
| Pre-dilated pressure (atm)                | 1.089 (0.992–1.196)             | .073         |                                  |              |
| Post-dilated balloon diameter (mm)        | 0.922 (0.575–1.478)             | .735         |                                  |              |
| Post-dilated pressure (atm)               | 1.188 (1.038–1.360)             | .012         | 1.081 (0.949–1.231)             | .241         |
| Target-vessel stent length (mm)           | 1.003 (0.991–1.015)             | .608         |                                  |              |
| MLD post PCI (mm)                         | 0.239 (0.110–0.518)             | \( \leq .001 \) | 1.330 (0.572–3.094)             | .508         |
| DS post PCI (%)                           | 1.090 (1.060–1.121)             | \( \leq .001 \) | 1.067 (1.036–1.100)             | \( \leq .001 \) |
| QFRv post PCI (%)                         | 0.048 (0.008–0.290)             | .001         | 2.382 (0.145–39.073)            | .543         |
| QFRi post PCI                             | \( 1.2 \times 10^{-7} \) (3.0 \times 10^{-9}–4.8 \times 10^{-6}) | \( \leq .001 \) | \( 1.7 \times 10^{-6} \) (5.3 \times 10^{-11}–5.6 \times 10^{-6}) | \( \leq .001 \) |
| B to V ratio                              | 0.152 (0.020–1.138)             | .067         |                                  |              |
| Imaging use (%)                           | 1.156 (0.667–2.004)             | .605         |                                  |              |
| CB use (%)                                | 1.068 (0.503–2.269)             | .864         |                                  |              |
| LAD (%)                                   | 0.439 (0.248–0.778)             | .005         | 0.383 (0.210–0.697)             | .002         |
| FV post PCI (m/s)                         | 15.642 (5.63–434.677)           | .105         |                                  |              |

Abbreviations: B to V, burr to vessel; CB, cutting balloon; CI, confidential interval; DS, diameter stenosis; FV, flow velocity; HR, hazard ratio; LAD, left anterior descending coronary artery; MLD, minimal luminal diameter; PCI, percutaneous coronary intervention; QFRi, quantitative flow ratio in a segment; QFRv, vessel quantitative flow ratio; TLF, target lesion failure.
have shown a significant association between the low FFR measurement post-PCI without RA and the high risk of clinical adverse events at mid- and long-term follow-up.19–22 Due to different sensitive points of pressure wire location in the target vessel, FFR measurement of the target vessel would be influenced not only by the stent segment and the non-stent segment but also by the distal vessel disease and microcirculatory dysfunction. Therefore, a wide range of cutoff values of FFR post-PCI were described in different studies. The physiological function test of a moderate coronary lesion is a significant indication for PCI guidance in the current clinical practice.23 FFR has shown an outstanding value for predicting the late outcome post-PCI in a number of previous studies not only for single-vessel disease but also for multivessel disease. Considering the complex manipulation of FFR measurement by the pressure wire, the utilization rate is currently very low. A retrospective study of the physiological function is impossible if FFR measurement was not performed during the previous procedure; in contrast, it can still be done with the QFR appearance if the previous CAG quality meets the measuring requirements.

Compared with non- or mildly calcified lesions, moderately or severely calcified lesions with/without RA led to poor clinical outcomes in previous studies, even though the second-generation DES was used. This is because the lesion was poorly prepared, causing the stent underexpansion and malposition. RA may improve these scenarios, but it still fails to correlate with optimized clinical outcomes. In the present study, we measured two kinds of QFR (QFRv and QFRi) to differentiate the stenting effect and residual lesion burden; we found a high correlation between low post-PCI QFRi and high TLF at the 3-year follow-up for patients who underwent RA, which is consistent with previous studies without RA.13,19–22 The optimal cutoff value of QFRi post-PCI was 0.94 based on the ROC curve analysis, which is slightly high compared with the findings of the previous studies without RA (QFR: 0.85–0.92).13 The difference was likely caused by the inconsistency in observational indicators and clinical endpoints among different studies. Previous studies have mainly focused on the correlation between FFR/QFRv and MACE, while we primarily observed the correlation between QFRi and TLF. Patients with heavily calcified lesions after RA were more likely to have insufficient stent expansion and apposition than patients with non- or mildly calcified lesions. Such a suboptimal stent deployment would cause increased stent-related events. Therefore, the stent-related physiological index (QFRi) might predict late TLF more accurately than QFRv post-PCI.

LAD as the RA’s target vessel showed significantly low TLF compared with left circumflex artery (LCX) and right coronary artery (RCA) in our observational study. The reason might be that the sample size was small, and that the LAD’s RA was used more often in the non-TLF group than in the TLF group (83.1% vs. 65.4%). Low burr-to-vessel ratio causes a bad plaque modification, which leads to insufficient lesion preparation and stent underexpansion and malposition.4,24 High DS post-PCI is a predictor of in-stent restenosis and stent thrombosis.25 Therefore, in the present study, DS post PCI in the TLF group was notably high compared with that in the non-TLF group, and the burr-to-vessel ratio was likely to decrease in the TLF group. Additionally, the postdilated pressure of the balloon in the TLF group was higher than that in the non-TLF group, suggesting that the lesion preparation was insufficient in the TLF group. Still, DS post-PCI and postdilated pressure were both able to predict TLF in patients with heavily calcified lesions after RA at the 3-year follow-up by the univariate Cox regression analysis.

With the progress of interventional treatment of heavily calcified lesions, once the post-PCI QFR value is found to be less than the cutoff value from the present study, it is suggested to further use effective therapeutic methods, such as shockwave balloon, to improve the final post-PCI QFR value and achieve the optimization of therapy. Additionally, QFR measurement was very effective and

| Table 3 | The clinical outcome between the high- and low-QFR groups after about 3 years post-PCI |
|---------|---------------------------------|
|         | QFR > 0.94 (N = 170) | QFR ≤ 0.94 (N = 54) | p value |
| TLF (%) | 16 (9.4%) | 36 (66.7%) | ≤.001 |
| TL-CD (%) | 6 (3.5%) | 6 (11.1%) | .042 |
| TL-MI (%) | 5 (2.9%) | 11 (20.4%) | ≤.001 |
| TLR (%) | 10 (5.9%) | 30 (55.6%) | ≤.001 |

Note: Data were expressed as n (%).

Abbreviations: PCI, percutaneous coronary intervention; QFRi, quantitative flow ratio; TL-CD, target lesion-cardiac death; TL-MI, target lesion-myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization.
simple in predicting future clinical prognosis. Thus, it is recommended to provide routine post-PCI QFRi guidance for patients with complex PCI (such as RA) in daily practice. Based on the new concept suggested in the present study, the prospective randomized clinical trials should be designed in the future to treat patients with heavily calcified lesions using RA under the guidance of post-PCI QFRi.

4.1 | Limitations

This study had some limitations. First, our study was a retrospective study in which the imaging use ratio was about 50%, and <60% of the cases had clinical follow-up, and 50% of the cases had the angiographic follow-up. The reasons for this situation were the increased financial burden and unconventional clinical and CAG follow-up. Second, this study did not provide post-PCI FFR values. Finally, there was no established methodology for determining the QFR values of the stented segment.

5 | CONCLUSIONS

QFRi post-PCI showed a high predictive value for the long-term clinical outcome in patients who underwent RA during the PCI procedure. Besides, the lower QFRi post-PCI was associated with higher TLF. QFRi could be applied for evaluating the coronary stenting outcome in patients who underwent RA during the complex PCI.

ACKNOWLEDGEMENTS

We sincerely thank Shengxian Tu for supplying the AngioPlus QFR 1.0 software. This project was supported by Nanjing Municipal Science and Technology Bureau (grant number: 201803008), and Cardiocare Sponsored (CS) Optimized Antithrombotic Research Fund (grant number: BJUHFCSOARF201801-13).

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data in support of the results are available from the corresponding author on reasonable request.

ORCID

Fei Ye http://orcid.org/0000-0002-5651-3433

REFERENCES

1. Hansen DD, Auth DC, Vracko R, Ritchie JL. Rotational atherectomy in atherosclerotic rabbit iliac arteries. Am Heart J. 1988;115(1 Pt 1): 160-165.
2. Dill T. A randomized comparison of balloon angioplasty versus rotational atherectomy in complex coronary lesions (COBRA study). Eur Heart J. 2000;21(21):1759-1766.

3. Reifart N, Vandormael M, Krajcar M, et al. Randomized comparison of angioplasty of complex coronary lesions at a single center. Excimer Laser, Rotational Atherectomy, and Balloon Angioplasty Comparison (ERBAC) Study. Circulation. 1997;96(1):91-98.

4. Tomey MI, Kini AS, Sharma SK. Current status of rotational atherectomy. JACC Cardiovasc Interv. 2014;7(1):345-353.

5. Abdel-Wahab M, Richhardt G, Joachim Büttner H, et al. High-speed rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: the randomized ROTAXUS (Rotational Atherectomy Prior to Taxus Stent Treatment for Complex Native Coronary Artery Disease) trial. JACC Cardiovasc Interv. 2013;6(1):10-19.

6. Barbato E, Carrie D, Dardas P, et al. European expert consensus on rotational atherectomy. EuroIntervention. 2015;11(1):30-36.

7. Hoffmann R, Mintz GS, Kent KM, et al. Comparative early and nine-month results of rotational atherectomy, stents, and the combination of both for calcified lesions in large coronary arteries. Am J Cardiol. 1998;81(5):522-527.

8. de Waha S, Allali A, Büttner HJ, et al. Rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: Two-year clinical outcome of the randomized ROTAXUS trial. Catheter Cardiovasc Interv. 2016;87(4):691-700.

9. Lee JM, Hwang D, Choi KH, et al. Prognostic implications of relative increase and final fractional flow reserve in patients with stent implantation. JACC Cardiovasc Interv. 2018;11(20):2099-2109.

10. Tu S, Barbato E, Kószegi Z, et al. Fractional flow reserve calculation from 3-dimensional quantitative coronary angiography and TIMI frame count: a fast computer model to quantify the functional significance of moderately obstructed coronary arteries. JACC Cardiovasc Interv. 2014;7(7):768-777.

11. Tu S, Westra J, Yang J, et al. Diagnostic accuracy of fast computational approaches to derive fractional flow reserve from diagnostic coronary angiography: the international Multicenter FAVOR Pilot Study. JACC Cardiovasc Interv. 2016;9(19):2024-2035.

12. Westra J, Tu S, Campo G, et al. Diagnostic performance of quantitative flow ratio in prospectively enrolled patients: An individual patient-data meta-analysis. Catheter Cardiovasc Interv. 2019;94(5):693-701.

13. Biscaglia S, Tebaldi M, Brugalla S, et al. Prognostic value of QFR measured immediately after successful stent implantation: the International Multicenter Prospective HAWKEYE Study. JACC Cardiovasc Interv. 2019;12(20):2079-2088.

14. Xu B, Tu S, Qiao S, et al. Diagnostic accuracy of angiography-based quantitative flow ratio measurements for online assessment of coronary stenosis. J Am Coll Cardiol. 2017;70(25):3077-3087.

15. Ali RM, Abdul Kader M, Wan Ahmad WA, et al. Treatment of coronary drug-eluting stent restenosis by a sirolimus- or paclitaxel-coated balloon. JACC Cardiovasc Interv. 2019;12(6):559-566.

16. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction. J Am Coll Cardiol. 2018;72(18):2231-2264.

17. Mehran R, Dangas G, Abizaid AS, et al. Angiographic patterns of in-stent restenosis: classification and implications for long-term outcome. Circulation. 1999;100(18):1872-1878.

18. Vranckx P, Kint PP, Morel MA, van Es GA, Serruys PW, Cutlip DE. Identifying stent thrombosis, a critical appraisal of the academic research consortium (ARC) consensus definitions: a lighthouse and as a toe in the water. EuroIntervention. 2008;4Suppl C:C39-C44.

19. Li SJ, Ge Z, Kan J, et al. Cutoff value and long-term prediction of clinical events by FFR measured immediately after implantation of a drug-eluting stent in patients with coronary artery disease: 1- to 3-year results from the DKCRUSH VII Registry Study. JACC Cardiovasc Interv. 2017;10(10):986-995.

20. Lee JM, Koo BK, Shin ES, et al. Clinical implications of three-vascular fractional flow reserve measurement in patients with coronary artery disease. Eur Heart J. 2018;39(11):945-951.

21. Piroth Z, Toth GG, Tonino PAL, et al. Prognostic value of fractional flow reserve measured immediately after drug-eluting stent implantation. Circ Cardiovasc Interv. 2010;3(6):600-607.

22. Agarwal SK, Kasula S, Hacioglu Y, Ahmed Z, Uretsky BF, Hakeem A. Utilizing post-intervention fractional flow reserve to optimize acute results and the relationship to long-term outcomes. JACC Cardiovasc Interv. 2016;9(10):1022-1031.

23. Fearon WF, Nishi T, De Bruyne B, et al. Clinical outcomes and cost-effectiveness of fractional flow reserve-guided percutaneous coronary intervention in patients with stable coronary artery disease: three-year follow-up of the FAME 2 trial (fractional flow reserve versus angiography for multivessel evaluation). Circulation. 2018;137(5):480-487.

24. Barbato E, Dudek D, Haude M, et al. Mapping interventional cardiology in Europe: proceedings of the 3rd Summit of the European Association of Percutaneous Cardiovascular Interventions. EuroIntervention. 2015;11(1):27-28.

25. Cuculi F, Bossard M, Zasada W, et al. Performing percutaneous coronary interventions with predilatation using non-compliant balloons at high-pressure versus conventional semi-compliant balloons: insights from two randomised studies using optical coherence tomography. Open Heart. 2020;7(1):e001204.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher’s website.