Circulation Reports
Circ Rep 2022; 4: 439–446
doi:10.1253/circrep.CR-22-0069

ORIGINAL ARTICLE
Renal Disease

Differential Impact of Renal Function on the Diagnostic Performance of Resting Full-Cycle Ratio in Patients With Renal Dysfunction

Hirofumi Ohashi, MD, PhD; Tomoaki Nawano, MD; Hiroaki Takashima, MD, PhD; Hirohiko Ando, MD, PhD; Reiji Goto, MD, PhD; Akihiro Suzuki, MD, PhD; Shinichiro Sakurai, MD, PhD; Wataru Suzuki, MD; Yusuke Nakano, MD, PhD; Hiroaki Sawada, MD; Masanobu Fujimoto, MD; Koshiro Sakai, MD, PhD; Yasushi Suzuki, MD, PhD; Katsuhisa Waseda, MD, PhD; Tetsuya Amano, MD, PhD

Background: Physiological assessments using fractional flow reserve (FFR) and resting full-cycle ratio (RFR) have been recommended for revascularization decision making. Previous studies have shown a 20% rate of discordance between FFR and RFR. In this context, the correlation between RFR and FFR in patients with renal dysfunction remains unclear. This study examined correlations between RFR and FFR according to renal function.

Methods and Results: In all, 263 consecutive patients with 370 intermediate lesions were enrolled in the study. Patients were classified into 3 groups according to renal function: Group 1, estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m^2; Group 2, 30 mL/min/1.73 m^2≤eGFR<60 mL/min/1.73 m^2; Group 3, eGFR <30 mL/min/1.73 m^2. The discordance between FFR and RFR was assessed using known cut-off values for FFR (≤0.80) and RFR (≤0.89). Of the 370 lesions, functional significance with FFR was observed in 154 (41.6%). RFR was significantly correlated with FFR in all groups (Group 1, R^2=0.62 [P<0.001]; Group 2, R^2=0.67 [P<0.001]; Group 3, R^2=0.46 [P<0.001]). The rate of discordance between RFR and FFR differed significantly among the 3 groups (Group 1, 18.8%; Group 2, 18.5%; Group 3, 42.9%; P=0.02).

Conclusions: The diagnostic performance of RFR differed based on renal function. A better understanding of the clinical factors contributing to FFR/RFR discordance, such as renal function, may facilitate the use of these indices.

Key Words: Chronic kidney disease; Coronary artery disease; Fractional flow ratio; Resting full-cycle ratio

Clinical Perspective

What Is New?

This study is the first to focus on the correlation between RFR and FFR in patients with renal dysfunction.

The rate of discordance between RFR and FFR differed significantly according to renal function.

What Are the Clinical Implications?

Coronary artery disease (CAD) in patients with chronic kidney disease has been associated with an increased risk of death. Therefore, the importance of intervention strategies in patients with CAD complicated by renal dysfunction should be considered.

RFR had the lowest correlation with FFR in patients with renal dysfunction. When making decisions regarding percutaneous coronary intervention in patients with severe renal dysfunction, careful consideration is required.

Fractional flow reserve (FFR) is the gold standard for evaluating functional lesion severity in daily clinical practice.[1–4] The instantaneous wave-free ratio (iFR), which does not require hyperemic conditions, has been shown to be non-inferior to FFR as a physiological index in 2 large randomized controlled trials.[5,6] The resting full-cycle ratio (RFR) is a novel resting index that does not require hyperemic conditions. The RFR is measured as the maximum

Received July 25, 2022; accepted July 25, 2022; J-STAGE Advance Publication released online August 24, 2022 Time for primary review: 1 day
Department of Cardiology (H.O., T.N., H.T., H.A., R.G., A.S., S.S., W.S., Y.N., H.S., M.F., Y.S., K.W., T.A.), Medical Education Center (K.W.), Aichi Medical University, Nagakute; Department of Medicine, Division of Cardiology, Showa University School of Medicine, Tokyo (K.S.), Japan
The first two authors contributed equally to this work (H.O., T.N.).
Mailing address: Hiroaki Takashima, MD, PhD, FESC, FJCS, Department of Cardiology, Aichi Medical University, 1-1 Yazakokarimata, Nagakute 480-1195, Japan. E-mail: h0914@aichi-med-u.ac.jp
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ISSN-2434-0790

relative pressure difference during the entire cardiac cycle, regardless of systole or diastole, and is thus completely independent of electrocardiographic findings.[7] Previous studies have shown that the RFR is well correlated with and has good diagnostic accuracy for FFR and iFR in clinical practice.[8–10] However, discordant results between the RFR and FFR have been observed to occur in approximately 20% of cases, which can lead to confusion when making revascularization decisions.[11,12]

Coronary artery disease (CAD) is the leading cause of death in patients with chronic kidney disease (CKD).[13] The presence of kidney disease is associated with an increased risk of procedural complications (including renal injury) from coronary angiography and revascularization, death, myocardial infarction (MI), stent thrombosis, and bleeding complications of percutaneous coronary interventions (PCI).[14] CKD had an additive effect on adverse long-term outcomes in patients receiving PCI.[15] These data demonstrate the importance of intervention strategies in patients with CAD complicated by renal dysfunction. Therefore, the severity of functional lesions should be carefully assessed in patients with CKD.

It is unclear whether the diagnostic performance of RFR for detecting functional ischemia is similar, regardless of the degree of renal function. The aim of this study was to clarify the correlation between RFR and FFR according to renal function.

Methods

Study Design and Patient Population

This retrospective observational study was conducted at the Aichi Medical University Hospital in Japan. From August 2018 to February 2021, consecutive patients with intermediate coronary lesions who underwent elective coronary angiography and invasive physiological assessments were prospectively enrolled in the study. The primary aim of the study was to clarify the correlation between RFR and FFR according to renal function.

This study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the Aichi Medical University Hospital, Nagakute, Japan (Approval no. 2019-057), and written informed consent was obtained from all patients.

Angiographic Analysis and Quantitative Coronary Angiography (QCA)

Coronary angiography with a 5-Fr guiding catheter without side holes was performed through the radial or femoral artery, according to standard techniques. All patients were pretreated with intracoronary nitrate (100 or 200 μg) before angiography. A computerized quantitative analysis system using QCA software (CAAS 5.9; Pie Medical Imaging, Maastricht, Netherlands) was used for automated contour detection and quantification by 2 experienced observers blinded to the results of the RFR and FFR assessments. The reference vessel diameter, minimum lumen diameter, percentage diameter stenosis (%DS), and lesion length were measured using the external diameter of the contrast-filled 5-Fr guiding catheter for calibration. The %DS was measured in the most severe lesion at the end of diastole. QCA measurements were performed according to the Japanese Association of Cardiovascular Intervention and Therapeutics QCA Expert Document.[8]

Coronary Physiological Measurements and Assessments

All coronary physiological measurements were performed after the diagnostic angiography. The pressure wire (PressureWire™ X guidewire; Abbott Vascular, Santa Clara, CA, USA) was advanced distally to a segment of the target vessel before it was zeroed and equalized to the aortic pressure. An intracoronary bolus of nitrate (100 or 200 μg) was administered before each set of physiological measurements. In patients with multivessel disease, measurements were taken in each vessel with sufficient time intervals between measurement. First, the RFR was directly and automatically calculated online using the QUANTIEN system (Abbott Vascular). Second, the FFR was measured at maximum hyperemia with continuous infusion of ATP (180 μg/kg/min) through a peripheral vein. After all measurements were taken, the pressure sensor located at the tip of the guiding catheter was used to check for the presence of pressure drift.[16] RFR was defined as the lowest distal coronary-to-aortic pressure value for each heartbeat averaged over 5 heart cycles and could be captured in snapshot mode.

Cut-Off Values for Physiological Indices and Lesion Classification

Cut-off values of 0.89 and 0.80 were used for RFR and FFR, respectively. The FFR was adopted as a reference standard for estimating the functional significance of coronary artery stenosis.

CKD Classification and Hemodialysis Status

Patients were classified into 3 groups according to renal function: Group 1, estimated glomerular filtration rate (eGFR) $\geq$60 mL/min/1.73 m^2; Group 2, 30 mL/min/1.73 m^2$\leq$eGFR $<$60 mL/min/1.73 m^2; Group 3, eGFR $<$30 mL/min/1.73 m^2. CKD stages were determined according to the Kidney Disease: Improving Global Outcomes Group (KDIGO) 2012 guidelines.[17] We included hemodialysis patients in this study. All hemodialysis patients were adults (age $\geq$18 years) on maintenance dialysis for $\geq$90 days and had a stable dialysis prescription for $\geq$30 days. Hemodialysis patients underwent physiological measurements and blood sampling on non-dialysis days.

Statistical Analysis

Data for continuous variables are expressed as mean$\pm$SD or median and interquartile range. Categorical variables are expressed as numbers and percentages. Continuous variables were compared using the unpaired Student's t-test, and categorical variables were compared using the Chi-squared or Fisher's exact test, as appropriate. The Bonferroni method was used to correct for multiple comparisons. Mann-Whitney U-tests were used for non-parametric data. Pearson's correlation with the coefficient of determination (R) and linear regression analyses were used to examine the relationship between the RFR and FFR. Receiver operating characteristic (ROC) curve analysis was used to examine RFR agreement. Using FFR $\leq$0.80 (reference RFR) as a reference standard, an optimal cut-off was determined using Youden's index, and the area under the curve (AUC) was calculated. The Cochran-Armitage trend test was used to assess whether a trend was present between a variable with 2 categories and a variable with multiple categories. Statistical significance was set at 2-tailed $P<0.05$.

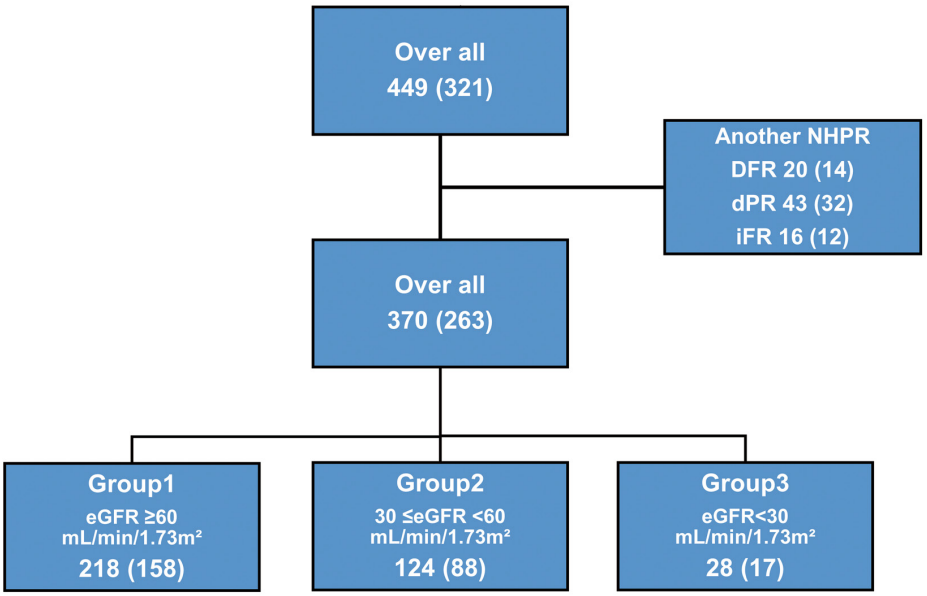

Figure 1. Study population. DFR, diastolic hyperemia-free ratio; dPR, diastolic pressure ratio; eGFR, estimated glomerular filtration rate; iFR, instantaneous wave-free ratio; NHPR, non-hyperemic pressure ratio.

Table 1. Baseline Patient Characteristics

	Overall (n=263)	Group 1 (n=158)	Group 2 (n=88)	Group 3 (n=17)	P value
Age (years)	73.0 [66.5–78.0]	71.0 [62.0–78.0]	71.1 [71.0–79.0]	71.2 [66.5–75.0]	0.001
Male sex	201 (76.4)	118 (74.7)	71 (80.7)	12 (70.6)	0.48
Hypertension	195 (74.7)	114 (72.6)	69 (79.3)	12 (70.6)	0.47
Diabetes	112 (42.6)	63 (39.9)	39 (44.3)	10 (58.8)	0.30
Dyslipidemia	186 (71.3)	114 (72.6)	65 (74.7)	7 (41.2)	0.02
Current smoker	113 (43.8)	80 (51.6)	25 (29.1)	8 (47.1)	0.003
Hemodialysis	14 (5.4)	0 (0.6)	0 (0.0)	14 (82.4)	<0.001
Medication					
Aspirin	217 (82.5)	135 (85.4)	71 (80.7)	11 (64.7)	0.09
Thienopyridine	69 (26.2)	38 (24.1)	27 (30.7)	4 (23.5)	0.51
β-blocker	108 (41.2)	64 (40.8)	36 (40.9)	8 (41.2)	0.88
Calcium channel blocker	110 (42.0)	64 (40.8)	35 (39.8)	11 (64.7)	0.14
Statin	199 (75.7)	124 (78.5)	66 (75.0)	9 (52.9)	0.07
Insulin	10 (3.8)	6 (3.8)	2 (2.3)	2 (11.8)	0.14
Hb (g/dL)	13.6 [12.4–14.7]	14.0 [12.9–15.0]	13.2 [12.0–14.6]	11.8 [10.4–13.0]	<0.001
eGFR (mL/min/1.73 m²)	64.2 [52.0–78.3]	74.5 [66.8–87.0]	51.4 [46.9–55.0]	7.14 [5.8–17.4]	<0.001
Cr (mg/dL)	0.85 [0.71–1.05]	0.73 [0.65–0.85]	1.07 [0.96–1.17]	6.84 [3.17–8.05]	<0.001

Categorical variables are presented as n (%) and continuous variables are presented as the mean ± SD or median [interquartile range]. *Variables used for multivariable analyses comparing hazard ratios of symptomatic and asymptomatic patients for the study endpoints. Group 1, estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m²; Group 2, 30 mL/min/1.73 m²≤eGFR<60 mL/min/1.73 m²; Group 3, eGFR <30 mL/min/1.73 m²; Cr, creatinine; Hb, hemoglobin.

Results

Study Population

There were 263 patients (370 lesions) included in this study; Group 1 consisted of 158 patients (218 lesions), Group 2 consisted of 88 patients (124 lesions), and Group 3 consisted of 17 patients (28 lesions; **Figure 1**).

Patient and Lesion Characteristics

Baseline clinical and lesion characteristics are presented in **Tables 1** and **2**. The median age of patients was 73.0 years and 76.4% were male. Functional significance was observed in 154 lesions (41.6%). Median serum creatinine and eGFR values were 0.85 mg/dL and 64.2 mL/min/1.73 m², respectively. There was a significant difference among the 3 groups

Table 2. Baseline Lesion Characteristics

	Overall (n=370)	Group 1 (n=218)	Group 2 (n=124)	Group 3 (n=28)	P value
Target vessel					
Left main trunk	10 (2.7)	6 (2.8)	4 (3.2)	0 (0.0)	0.89
Left anterior descending	193 (52.2)	115 (52.8)	64 (54.6)	14 (50.0)	0.95
Left circumflex	75 (20.3)	43 (19.7)	25 (20.2)	7 (25.0)	0.81
Right coronary artery	88 (23.8)	52 (23.9)	30 (24.2)	6 (21.4)	0.95
Quantitative coronary analysis results					
Reference vessel diameter (mm)	2.82 [2.39–3.34]	2.90 [2.35–3.46]	2.91 [1.29–1.87]	2.88 [2.20–3.72]	0.67
Minimum lumen diameter (mm)	1.73 [1.26–2.26]	1.59 [1.20–1.94]	1.29 [1.62–1.87]	1.71 [1.14–1.91]	0.85
Diameter stenosis (%)	46.4±13.6	45.5±13.8	47.7±12.3	47.5±16.9	0.32
Lesion length (mm)	11.69 [8.01–16.40]	11.7 [7.4–16.0]	10.7 [8.0–14.8]	7.82 [6.31–11.5]	0.10
FFR	0.82 [0.76–0.88]	0.83 [0.76–0.89]	0.81 [0.75–0.88]	0.82 [0.75–0.89]	0.39
RFR	0.91 [0.87–0.96]	0.92 [0.88–0.96]	0.91 [0.85–0.95]	0.88 [0.82–0.91]	0.009

Categorical variables are presented as n (%) and continuous variables are presented as the mean±SD or median [interquartile range]. *Variables used for multivariable analyses comparing hazard ratio of symptomatic and asymptomatic patients for the study endpoints. Group 1, estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m^2; Group 2, 30 mL/min/1.73 m^2≤eGFR<60 mL/min/1.73 m^2; Group 3, eGFR <30 mL/min/1.73 m^2; FFR, fractional flow reserve; RFR, resting full-cycle ratio.

in serum creatinine (0.73, 1.07, and 6.84 mg/dL in Groups 1, 2 and 3, respectively; P<0.001) and eGFR (74.5, 51.4, and 7.14 mL/min/1.73 m^2 in Groups 1, 2 and 3, respectively; P<0.001). Of the 260 patients in this study, 14 underwent hemodialysis. All hemodialysis patients were in Group 3 (**Table 1**).

In terms of lesion distribution, left main trunk (LM) and left anterior descending coronary artery (LAD) lesions were observed in 54.9% of the cohort. The mean angiographic %DS was 46.4±13.6%. The median FFR and RFR values were 0.82 and 0.91, respectively.

Lesion characteristics were not significantly different among the 3 groups, except for RFR (0.92, 0.91, and 0.88 in Groups 1, 2 and 3, respectively; P<0.001; **Table 2**).

Relationship Between RFR and FFR Values

There was a good correlation between RFR and FFR values for all lesions (R^2=0.59; 95% confidence interval [CI] 0.73–0.81; P<0.001; **Supplementary Figure 1**). After stratification according to renal function, the significant correlation between RFR and FFR remained in all groups: Group 1, R^2=0.62, 95% CI 0.73–0.84, P<0.001; Group 2, R^2=0.67, 95% CI 0.75–0.87, P<0.001; and Group 3, R^2=0.46, 95% CI 0.40–0.84, P<0.001, respectively) (**Figure 2A**,**2C**,**2E**). ROC curves of RFR values for an FFR cut-off value of 0.80 showed good AUCs in all groups: Group 1, 0.89 (95% CI, 0.84–0.93); Group 2, 0.87 (95% CI 0.81–0.93); and Group 3, 0.73 (95% CI 0.53–0.92) (**Figure 2B**,**2D**,**2F**).

Discordant Results Between RFR and FFR

Of all lesions, 20.5% showed discordant results between the RFR and FFR (FFR >0.80 and RFR ≤0.89: 10.2%; FFR ≤0.80 and RFR >0.89: 10.2%). The prevalence of discordance between the RFR and FFR differed significantly among the 3 groups (Group 1, 18.8%; Group 2, 18.5%; Group 3, 42.9%; P=0.02), with discordant results significantly higher in Group 3 than in Group 1 (P=0.02) and Group 2 (P=0.03; **Figure 3A**). Of all the discordant results, 50% were positive for RFR and negative for FFR; the highest frequency of positive RFR and negative FFR was 75.0% (**Supplementary Figure 2**).

Discordant Results Between RFR and FFR Stratified According to CKD Stage

Patients were stratified into CKD stages based on the KDIGO 2012 guidelines, ranging from G1 (normal or high eGFR) to G5 (kidney failure).[17] The highest prevalence of discordance between RFR and FFR was 42.9% in G5, whereas the lowest prevalence of discordance was 15.8% in G1. The frequency of discordance between RFR and FFR increased significantly as the CKD stage worsened.

Discussion

The main findings of the present study are that: (1) there is high concordance between RFR and FFR in detecting physiological significance regardless of renal dysfunction; (2) the rate of discordant results between RFR and FFR was significantly higher in patients with renal dysfunction (eGFR <30 mL/min/1.73 m^2); and (3) discordance between RFR and FFR was more likely observed in the setting of impaired kidney function. To the best of our knowledge, this is the first study to focus on the correlation between RFR and FFR in patients with renal dysfunction.

Discordant Results Between RFR and FFR in Patients With Renal Dysfunction

In the present study, RFR was positively correlated with FFR (R^2=0.59), which is consistent with results reported by previous studies (R^2=0.44–0.59).[8,10,12] When we stratified patients according to renal function, the lowest correlation between RFR and FFR was observed in the group with renal dysfunction (eGFR ≥60 mL/min/1.73 m^2, R^2=0.62; 30 mL/min/1.73 m^2≤eGFR<60 mL/min/1.73 m^2, R^2=0.67; eGFR <30 mL/min/1.73 m^2, R^2=0.46; P<0.001).

In this study, 20.5% of lesions showed discordant results between RFR and FFR, which is consistent with previous reports (discordance rate 13.1–27.4%).[7,10–12,18] The highest frequency of discordant results (42.9%) was observed in Group 3 (eGFR <30 mL/min/1.73 m^2). Most cases of discordance resulting in renal dysfunction had a positive RFR and negative FFR (75.0%). With regard to CKD stage, the frequency of discordant results was higher in

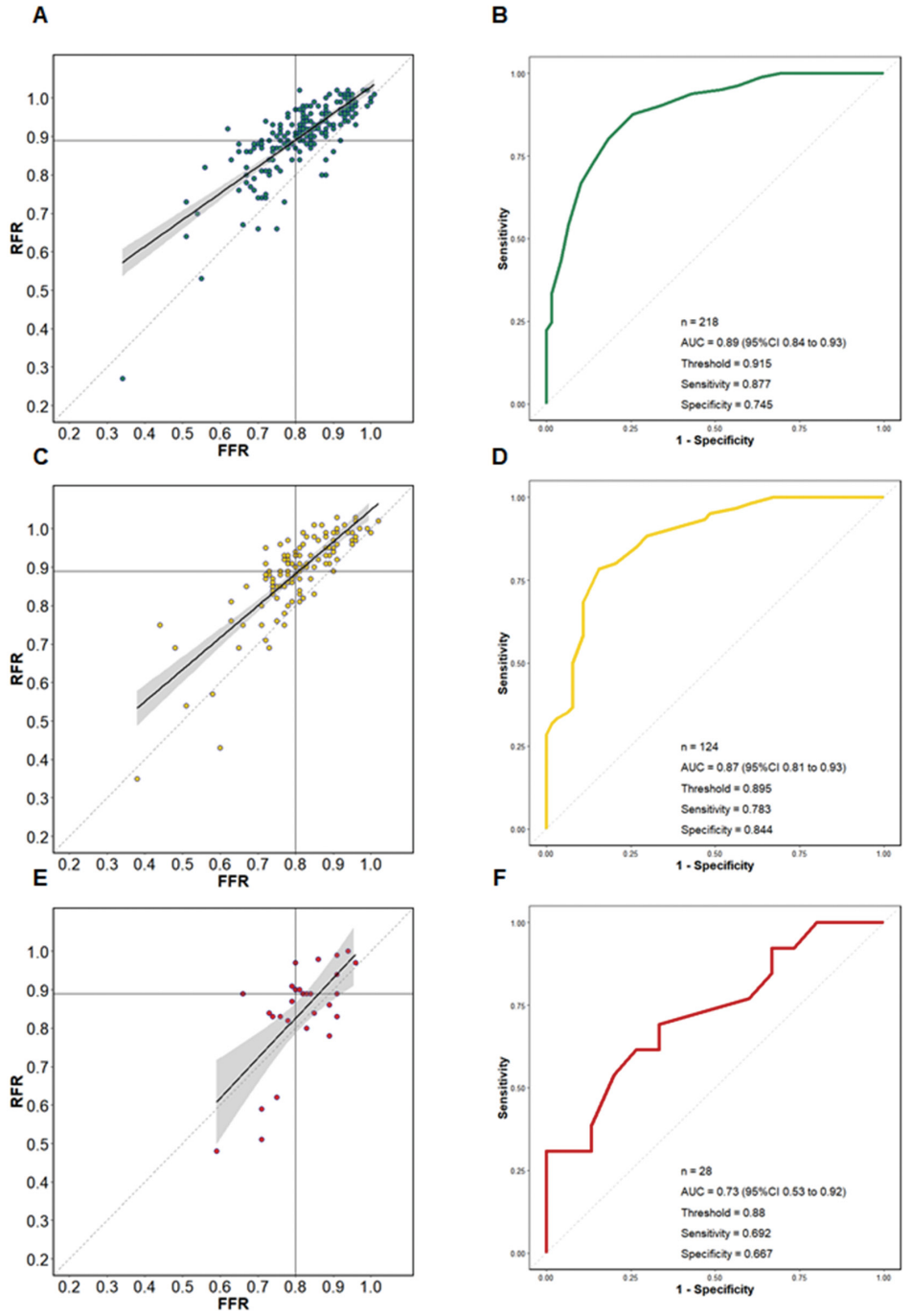

Figure 2. Relationship between resting full-cycle ratio (RFR) and fractional flow reserve (FFR) in (**A**,**B**) Group 1 (estimated glomerular filtration rate [eGFR] ≥60 mL/min/1.73 m^2), (**C**,**D**) Group 2 (30 mL/min/1.73 m^2≤eGFR<60 mL/min/1.73 m^2), and (**E**,**F**) Group 3 (eGFR <30 mL/min/1.73 m^2). (**A**,**C**,**E**) Correlation plots between RFR and FFR. (**B**,**D**,**F**) Receiver operating characteristic (ROC) curves of RFR values for an FFR cut-off value of 0.80. AUC, area under the curve; CI, confidence interval.

Stage G3b patients than in Stage G1–G3a patients. Thus, when evaluating CAD patients with moderate renal function dysfunction using FFR and RFR, care should be taken when interpreting the results. It is interesting that the frequency of discordant results between the RFR and FFR tended to increase as the CKD stage worsened.

Mechanism of Discordance Between RFR and FFR in Patients With Renal Dysfunction

The difference between RFR and FFR is the method of physiological measurement (i.e., hyperemic or non-hyperemic).[7,19] The FFR is an index of the effect of epicardial coronary artery stenosis on maximum myocardial perfu-

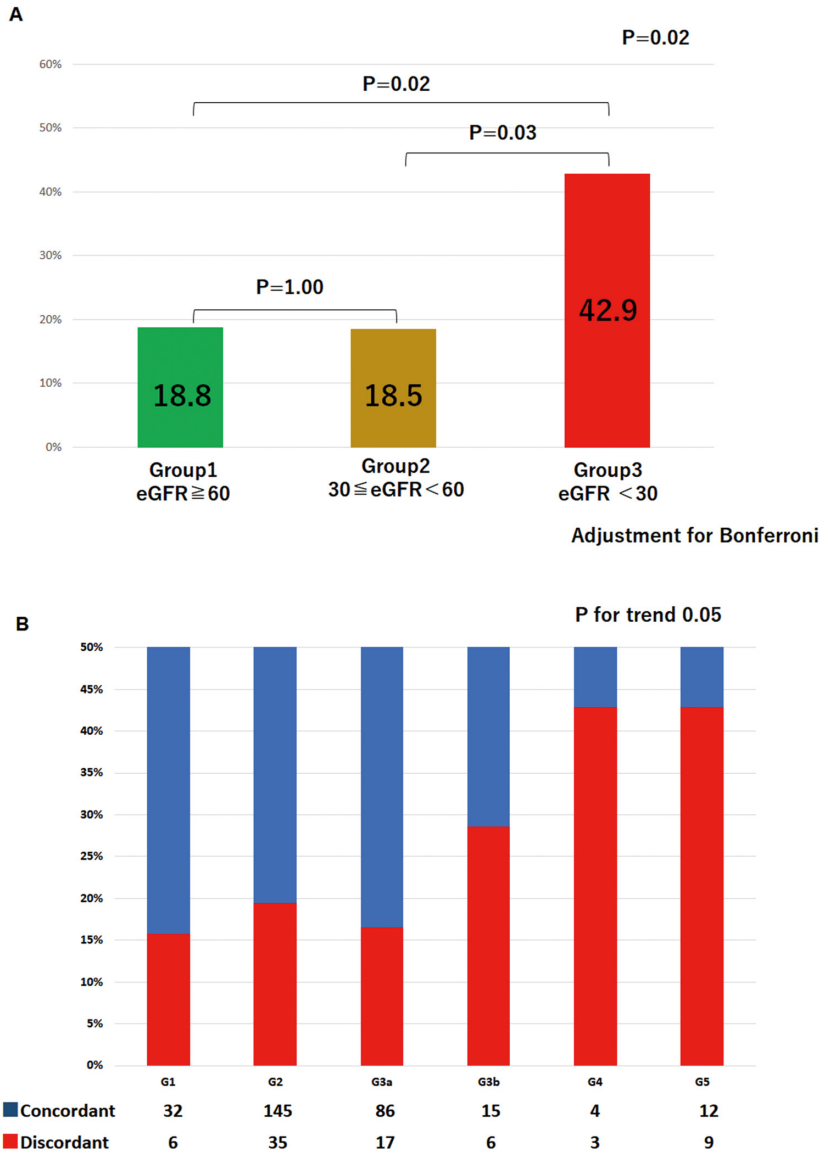

Figure 3. Rates of discordance between resting full-cycle ratio (RFR) and fractional flow reserve (FFR) according to (**A**) renal function after Bonferroni correction and (**B**) chronic kidney disease (CKD) stage. The CKD stages were as follows: G1, estimated glomerular filtration rate (eGFR) ≥90 mL/min/1.73 m^2; G2, 60 mL/min/1.73 m^2≤eGFR<89 mL/min/1.73 m^2; G3a, 45 mL/min/1.73 m^2≤eGFR<59 mL/min/1.73 m^2; G3b, 30 mL/min/1.73 m^2≤eGFR<44 mL/min/1.73 m^2; G4, 15 mL/min/1.73 m^2≤eGFR<29 mL/min/1.73 m^2; G5, eGFR <15 mL/min/1.73 m^2.

sion.[19] Conversely, the non-hyperemic pressure ratio (NHPR), including RFR, is evaluated during resting conditions.[7,20] Previous studies reported that several predictors, such as patient and lesion characteristics, were associated with differences in results between NHPR and FFR.[10–12,21,22] These predictors can be attributed to factors affecting coronary flow reserve (CFR), such as the presence of microvascular dysfunction and differences in coronary resting flow velocity. Compared with FFR, NHPR showed a stronger correlation and better agreement with CFR.[23] Previous studies have shown that CFR is significantly associated with CKD stage, declining in early CKD.[24,25] In addition, it has been reported that renal dysfunction, such as the need for hemodialysis, is an independent predictor of discordant results between RFR and FFR.[11,12] This mechanism can be explained by a high coronary flow velocity or low CFR with microvascular dysfunction. Due to the low CFR, there is a possibility of false-positive RFR results (positive RFR and negative FFR). Our results support the hypothesis that most cases of discordance resulting in renal dysfunction in Group 3 had a positive RFR and negative FFR (75.0%).

Clinical Implications

CAD in patients with CKD has been associated with an increased risk of death. The effectiveness of PCI in patients with renal dysfunction is still not clear. Kuramitsu et al demonstrated the long-term safety of FFR-based deferral of revascularization in patients with chronic coronary syndrome. However, the 5-year follow-up of the J-CONFIRM Registry demonstrated that hemodialysis was strongly associated with 5-year target vessel failure.[3,4] Furthermore, a previous report did not find any evidence that an initial invasive strategy, compared with an initial conservative strategy, reduced the risk of death or non-fatal MI among patients with stable coronary disease, advanced CKD, and moderate or severe ischemia.[26] Moderate CKD was independently associated with insufficient improvement in

FFR after stent implantation.[27] Furthermore, RFR may overestimate coronary ischemia with a low CFR, such as in renal dysfunction, compared with FFR. Therefore, the initial conservative strategy for patients with renal dysfunction based on RFR should be carefully considered.

In the present study, RFR had the lowest correlation with FFR in patients with renal dysfunction. The frequency of discordant results between RFR and FFR increased significantly as the CKD stage worsened. Therefore, the importance of intervention strategies in patients with CAD complicated by renal dysfunction should be considered, and clinical studies are warranted to compare outcomes after clinical decision making based on FFR and NHPR.

Study Limitations

This study has several limitations. First, this was a retrospective observational study and we only included consecutive patients within a certain period. Second, this was a single-center study with a small sample size. Therefore, this study may have been underpowered to demonstrate discordant results in patients with renal dysfunction. Further large-scale studies are required to confirm the validity of our results. Third, we also included patients with factors that were deemed to affect physiological measurements, such as diabetes, impaired cardiac function, LM and LAD lesions, and the use of β-blockers. Although these patients were excluded from previous studies, we considered it important to directly compare RFR and FFR in these patients in a real-world setting. Fourth, we included patients undergoing hemodialysis. Patients undergoing hemodialysis have an unstable physiological condition that is affected not only by renal dysfunction, but also by other factors, such as central venous pressure and high coronary velocity. However, the impact of these factors on FFR in patients undergoing hemodialysis is still not clear. We considered it important to directly compare RFR and FFR, including in patients undergoing hemodialysis, in a real-world setting. Finally, because we did not evaluate the clinical outcomes between RFR and FFR, we could not determine whether RFR or FFR is better for decision making regarding coronary revascularization in cases with discordant results. Further large clinical outcome studies are warranted to elucidate treatment strategies for lesions with discordant results between RFR and FFR.

Conclusions

The diagnostic performance of RFR differed depending on renal function. A better understanding of the clinical factors that contribute to FFR/RFR discordance, such as renal function, may make a considerable contribution to the use of these indices.

Acknowledgments

The authors thank all the staff and patients who contributed to this study.

Sources of Funding

This study did not receive any specific funding.

Disclosures

The authors have no conflicts of interest to declare.

IRB Information

This study was approved by the Ethics Committee of Aichi Medical University Hospital (Reference no. 2019-057). Informed consent was obtained from all participants included in the study.

Data Availability

The deidentified participant data will not be shared.

References

1. Pijls NH, van Schaardenburgh P, Manoharan G, Boersma E, Bech JW, van't Veer M, et al. Percutaneous coronary intervention of functionally nonsignificant stenosis: 5-year follow-up of the DEFER Study. *J Am Coll Cardiol* 2007; **49:** 2105–2111.
2. Pijls NH, Fearon WF, Tonino PA, Siebert U, Ikeno F, Bornschein B, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention in patients with multivessel coronary artery disease: 2-year follow-up of the FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study. *J Am Coll Cardiol* 2010; **56:** 177–184.
3. Kuramitsu S, Matsuo H, Shinozaki T, Horie K, Takashima H, Terai H, et al. Two-year outcomes after deferral of revascularization based on fractional flow reserve: The J-CONFIRM Registry. *Circ Cardiovasc Interv* 2020; **13:** e008355.
4. Kuramitsu S, Matsuo H, Shinozaki T, Horie K, Takashima H, Terai H, et al. Five-year outcomes after fractional flow reserve-based deferral of revascularization in chronic coronary syndrome: Final results from the J-CONFIRM Registry. *Circ Cardiovasc Interv* 2022; **15:** e011387.
5. Davies JE, Sen S, Dehbi HM, Al-Lamee R, Petraco R, Nijjer SS, et al. Use of the instantaneous wave-free ratio or fractional flow reserve in PCI. *N Engl J Med* 2017; **376:** 1824–1834.
6. Gotberg M, Christiansen EH, Gudmundsdottir IJ, Sandhall L, Danielewicz M, Jakobsen L, et al. Instantaneous wave-free ratio versus fractional flow reserve to guide PCI. *N Engl J Med* 2017; **376:** 1813–1823.
7. Svanerud J, Ahn JM, Jeremias A, van't Veer M, Gore A, Maehara A, et al. Validation of a novel non-hyperaemic index of coronary artery stenosis severity: The Resting Full-cycle Ratio (VALIDATE RFR) Study. *EuroIntervention* 2018; **14:** 806–814.
8. Ohashi H, Takashima H, Ando H, Suzuki A, Sakurai S, Nakano Y, et al. Clinical feasibility of resting full-cycle ratio as a unique non-hyperemic index of invasive functional lesion assessment. *Heart Vessels* 2020; **35:** 1518–1526.
9. Kumar G, Desai R, Gore A, Rahim H, Maehara A, Matsumura M, et al. Real world validation of the nonhyperemic index of coronary artery stenosis severity: Resting full-cycle ratio: RE-VALIDATE. *Catheter Cardiovasc Interv* 2020; **96:** E53–E58.
10. Muroya T, Kawano H, Hata S, Shinboku H, Sonoda K, Kusumoto S, et al. Relationship between resting full-cycle ratio and fractional flow reserve in assessments of coronary stenosis severity. *Catheter Cardiovasc Interv* 2020; **96:** E432–E438.
11. Goto R, Takashima H, Ohashi H, Ando H, Suzuki A, Sakurai S, et al. Independent predictors of discordance between the resting full-cycle ratio and fractional flow reserve. *Heart Vessels* 2021; **36:** 790–798.
12. Kato Y, Dohi T, Chikata Y, Fukase T, Takeuchi M, Takahashi N, et al. Predictors of discordance between fractional flow reserve and resting full-cycle ratio in patients with coronary artery disease: Evidence from clinical practice. *J Cardiol* 2021; **77:** 313–319.
13. Sarnak MJ, Amann K, Bangalore S, Cavalcante JL, Charytan DM, Craig JC, et al. Chronic kidney disease and coronary artery disease: JACC state-of-the-art review. *J Am Coll Cardiol* 2019; **74:** 1823–1838.
14. Santopinto JJ, Fox KA, Goldberg RJ, Budaj A, Pinero G, Avezum A, et al. Creatinine clearance and adverse hospital outcomes in patients with acute coronary syndromes: Findings from the global registry of acute coronary events (GRACE). *Heart* 2003; **89:** 1003–1008.
15. Lin MJ, Lee J, Chen CY, Huang CC, Wu HP. Chronic kidney disease and diabetes associated with long-term outcomes in patients receiving percutaneous coronary intervention. *BMC Cardiovasc Disord* 2017; **17:** 242.
16. Kawase Y, Matsuo H, Akasaka T, Shiono Y, Tanaka N, Amano T, et al. Clinical use of physiological lesion assessment using pressure guidewires: An expert consensus document of the Japanese Association of Cardiovascular Intervention and Therapeutics. *Cardiovasc Interv Ther* 2019; **34:** 85–96.
17. Levin A, Stevens PE. Summary of KDIGO 2012 CKD guideline: Behind the scenes, need for guidance, and a framework for moving forward. *Kidney Int* 2014; **85:** 49–61.

18. Lee JM, Rhee TM, Choi KH, Park J, Hwang D, Kim J, et al. Clinical outcome of lesions with discordant results among different invasive physiologic indices: Resting distal coronary to aortic pressure ratio, resting full-cycle ratio, diastolic pressure ratio, instantaneous wave-free ratio, and fractional flow reserve. *Circ J* 2019; **83:** 2210–2221.
19. Pijls NH, De Bruyne B, Peels K, Van Der Voort PH, Bonnier HJ, Bartunek J, et al. Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses. *N Engl J Med* 1996; **334:** 1703–1708.
20. Sen S, Escaned J, Malik IS, Mikhail GW, Foale RA, Mila R, et al. Development and validation of a new adenosine-independent index of stenosis severity from coronary wave-intensity analysis: Results of the ADVISE (ADenosine Vasodilator Independent Stenosis Evaluation) study. *J Am Coll Cardiol* 2012; **59:** 1392–1402.
21. Lee JM, Shin ES, Nam CW, Doh JH, Hwang D, Park J, et al. Discrepancy between fractional flow reserve and instantaneous wave-free ratio: Clinical and angiographic characteristics. *Int J Cardiol* 2017; **245:** 63–68.
22. Derimay F, Johnson NP, Zimmermann FM, Adjedj J, Witt N, Hennigan B, et al. Predictive factors of discordance between the instantaneous wave-free ratio and fractional flow reserve. *Catheter Cardiovasc Interv* 2019; **94:** 356–363.
23. Petraco R, van de Hoef TP, Nijjer S, Sen S, van Lavieren MA, Foale RA, et al. Baseline instantaneous wave-free ratio as a pressure-only estimation of underlying coronary flow reserve: Results of the JUSTIFY-CFR Study (Joined Coronary Pressure and Flow Analysis to Determine Diagnostic Characteristics of Basal and Hyperemic Indices of Functional Lesion Severity-Coronary Flow Reserve). *Circ Cardiovasc Interv* 2014; **7:** 492–502.
24. Murthy VL, Naya M, Foster CR, Hainer J, Gaber M, Dorbala S, et al. Coronary vascular dysfunction and prognosis in patients with chronic kidney disease. *JACC Cardiovasc Imaging* 2012; **5:** 1025–1034.
25. Charytan DM, Skali H, Shah NR, Veeranna V, Cheezum MK, Taqueti VR, et al. Coronary flow reserve is predictive of the risk of cardiovascular death regardless of chronic kidney disease stage. *Kidney Int* 2018; **93:** 501–509.
26. Bangalore S, Maron DJ, O'Brien SM, Fleg JL, Kretov EI, Briguori C, et al. Management of coronary disease in patients with advanced kidney disease. *N Engl J Med* 2020; **382:** 1608–1618.
27. Sakoda K, Tanaka N, Hokama Y, Hoshino K, Murata N, Yamashita J, et al. Association of moderate chronic kidney disease with insufficient improvement of fractional flow reserve after stent implantation. *Catheter Cardiovasc Interv* 2016; **88:** E38–E44.

Supplementary Files

Please find supplementary file(s);
http://dx.doi.org/10.1253/circrep.CR-22-0069