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ORIGINAL RESEARCH

Prognostic Value of Postpercutaneous Coronary Intervention Murray-Law-Based Quantitative Flow Ratio

Post Hoc Analysis From FLAVOUR Trial

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ABSTRACT

BACKGROUND Coronary physiology measured by fractional flow reserve (FFR) is superior to angiography for assessing the efficacy of percutaneous coronary intervention (PCI). Yet, the clinical adoption of post-PCI FFR is limited. Murray law-based quantitative flow ratio (μQFR) may represent a promising alternative, as it can quickly compute FFR from a single angiographic view.

OBJECTIVES The authors aimed to investigate the potential role of post-PCI μQFR in predicting clinical outcomes.

METHODS This was a post hoc blinded analysis of the FLAVOUR trial. Patients with angiographically intermediate lesions randomized 1:1 to receive FFR or intravascular ultrasound-guided PCI were included. Post-PCI μQFR was assessed in successfully stented vessels, blinded to clinical outcomes. Suboptimal physiological outcome post-PCI was defined a priori as post-PCI μQFR <0.90. The primary endpoint was 2-year target vessel failure, including cardiac death, target vessel myocardial infarction, and target vessel revascularization. Secondary endpoints included the diagnostic concordance of pre-PCI μQFR with FFR in the FFR-guidance arm.

RESULTS Post-PCI μQFR was successfully analyzed in 806 vessels from 777 participants (feasibility 97.0% [806 of 831]). Suboptimal physiological outcome post-PCI was identified in 24.7% (199 of 806) of vessels and post-PCI μQFR <0.90 was associated with higher risk of 2-year target vessel failure (6.1% [12 of 199] vs 2.7% [16 of 607]; HR: 2.45 [95% CI: 1.14-5.26]; $P = 0.022$). Pre-PCI μQFR was obtained in 877 of 919 vessels (feasibility 95.4%), showing 90% accuracy, 82% sensitivity, and 94% specificity for identifying physiologically significant stenosis defined by pre-PCI FFR ≤0.80.

CONCLUSIONS In patients with intermediate lesions who underwent PCI with contemporary imaging or physiology guidance, lower post-PCI μQFR values predict subsequent adverse events. (Fractional FLow Reserve And IVUS for Clinical OUtcomes in Patients With InteRmediate Stenosis [FLAVOUR]; NCT02673424) (JACC Asia. 2025;5:59-70)

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ABBREVIATIONS AND ACRONYMS

FFR = fractional flow reserve

IVUS = intravascular ultrasound

PCI = percutaneous coronary intervention

QFR = quantitative flow ratio

TVF = target vessel failure

TVR = target vessel revascularization

μQFR = Murray law-based quantitative flow ratio

Despite angiographically successful percutaneous coronary intervention (PCI), 20% to 40% of patients continue to experience recurrent angina within 1 year[1-5] and up to 50% at 5 years[6] following the index procedure. Physiological guidance using wire-based fractional flow reserve (FFR) was superior to angiography-based guidance for identifying hemodynamically significant lesions,[2] but adverse cardiac events still occur in up to 13.8%[2] at 1 year and 39%[4] at 5 years for successfully treated vessels by angiographic inspection.

Evidence has suggested that approximately one-third to two-thirds of patients have a suboptimal physiological outcome post-PCI, even when angiographic results appear satisfactory,[7-11] portending worse clinical outcomes.[7-20] This indicates that physiological assessment after PCI may represent a valuable tool for evaluating PCI efficacy and predicting future events. However, the clinical adoption of wire-based FFR or nonhyperemic pressure ratios remains very low worldwide.[21] It remains common practice to estimate resting flow and the absence of residual epicardial obstacles to maximal flow from visual inspection of the coronary angiogram, calling for PCI success entirely on a subjective basis.

Quantitative flow ratio (QFR) is an extensively validated image-based method for fast computation of FFR based on 3-dimensional angiographic reconstruction and fluid dynamic algorithms.[22] A QFR-guided strategy of lesion selection improved 1-year clinical outcomes compared with standard angiography guidance in a large randomized trial.[23] Several pilot studies also indicated the prognostic value of QFR immediately after PCI.[19,20,24-27] Recently, the QFR method was upgraded to incorporate Murray bifurcation fractal law, which allows FFR computation from a single angiographic view.[28] This Murray law-based quantitative flow ratio (μQFR) has shown improved feasibility and comparable diagnostic accuracy to traditional 3D-QFR,[29,30] being a promising tool for comprehensive physiological assessments both before and immediately after PCI. Yet, the prognostic value of post-PCI μQFR remains unknown.

In this study, we aimed to investigate whether blinded analysis of poststenting μQFR is associated with clinical outcomes in patients undergoing successful PCI with implantation of second-generation drug-eluting stents (DES) in the randomized FLAVOUR (Fractional FLow Reserve And IVUS for Clinical OUtcomes in Patients With InteRmediate Stenosis; NCT02673424) trial.

METHODS

STUDY DESIGN AND PATIENT POPULATION. This is a post hoc blinded analysis based on the FLAVOUR trial population.[31,32] FLAVOUR is an investigator-initiated, prospective, randomized, open-label trial designed to compare wire-based FFR-guided and intravascular ultrasound (IVUS)-guided PCI strategy conducted at 18 sites in Korea and China. From July 2016 to August 2019, a total of 1,682 patients evaluated for PCI for the treatment of angiographically intermediate stenosis

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(40%-70% diameter stenosis by visual estimation) were enrolled and randomized 1:1 to FFR guidance (n = 838) or IVUS guidance (n = 844).[31,32] In the FFR group, PCI was performed with an FFR ≤0.80; in the IVUS group, PCI was performed with either minimal lumen area ≤3 mm² or 3 to 4 mm² with a plaque burden of >70%. If necessary, the same tool (FFR or IVUS) according to randomization was used for post-PCI optimization, with the goal of achieving successful PCI according to the criteria specified in FLAVOUR trial (Supplemental Methodology).

Data from 2 arms were pooled for the present analysis. The present study performed blinded post hoc analysis of the data from the FLAVOUR trial. The FLAVOUR trial was approved by the Institutional Review Board of each hospital where patients were enrolled and was conducted in accordance with the principles of the Declaration of Helsinki. All patients provided written informed consent.

All anonymized angiographic data from 1,682 patients with 1820 vessels in FLAVOUR trial were screened and analyzed in an independent academic core laboratory (CardHemo, Med-X Research Institute, Shanghai Jiao Tong University). Post-PCI μQFR analysis was retrospectively performed in vessels with at least 1 PCI treated lesion (Supplemental Figure 1). A final single angiographic view after PCI was used for post-PCI μQFR assessment. Vessels would be excluded if post-PCI angiogram was not available, was not final, or had insufficient image quality with much overlap, foreshortening, incomplete contrast filling, or blurry lumen contours. Image screening and post-PCI μQFR analyses were performed blinded to clinical outcomes and/or FFR data. Only after μQFR analyses were completed and the database was locked were clinical outcomes and/or FFR data disclosed to the core laboratory. The association between post-PCI μQFR and clinical outcomes was investigated subsequently.

In FFR-guidance group, pre-PCI μQFR was also performed in both deferred and stented vessels blinded to FFR results and clinical outcomes. The diagnostic concordance of pre-PCI μQFR and wire-based FFR was evaluated to verify the accuracy of single-view μQFR analysis.

ACQUISITION OF CORONARY ANGIOGRAPHY, IVUS IMAGES, AND FFR MEASUREMENT. Details regarding the acquisition of angiography, IVUS images, and FFR measurements were specified in the Supplemental Methodology.

OUTCOMES AND DEFINITIONS. The primary outcome of the present study was target vessel failure (TVF) at 2 years after randomization, defined as a composite of cardiac death, target vessel myocardial infarction (MI), and target vessel revascularization (TVR). In the FLAVOUR trial, all clinical outcomes were adjudicated by an independent clinical-events committee in a blinded fashion in accordance with the Academic Research Consortium consensus.[33] Detailed definitions for each separate endpoint were described in the main study.[32] All anonymized analyses were performed without prior knowledge of events during follow-up.

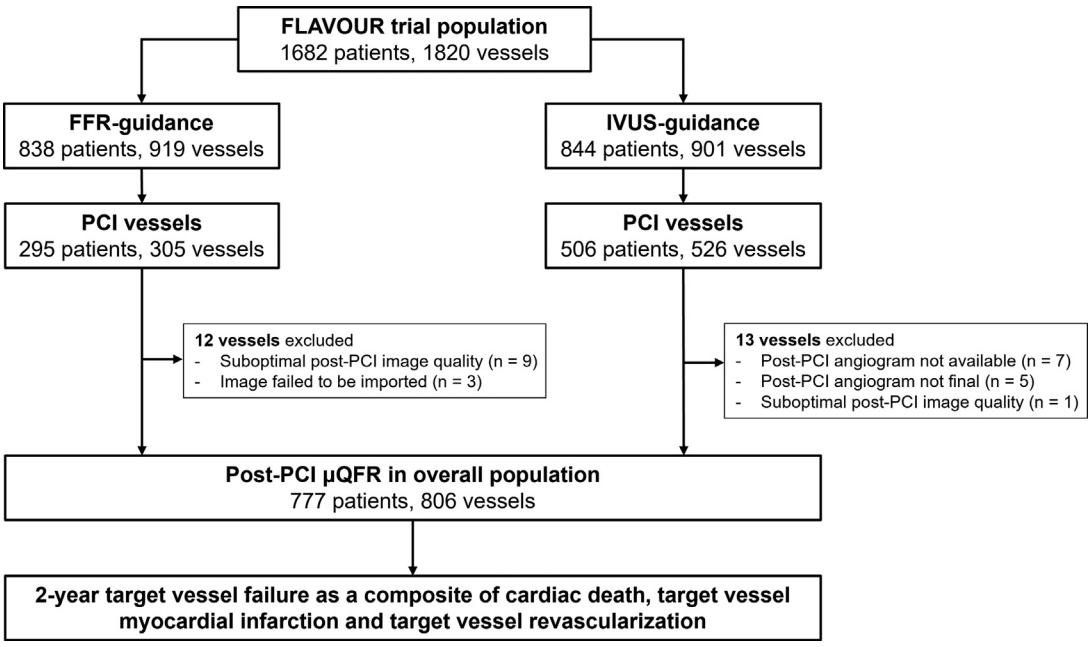
COMPUTATION OF μQFR. μQFR analyses were performed using the AngioPlus Core software (version V3, Pulse Medical) by experienced analysts who were certified for μQFR analysis. Post-PCI μQFR analyses were conducted by 2 analysts (D.D., H.S.) blinded to clinical outcome data and, when available, FFR values (Supplemental Figure 1). Pre-PCI μQFR analyses were performed in the FFR-guidance group by a third analyst (Z.W.) who was blinded to revascularization decision, clinical outcome data, FFR values, and post-PCI μQFR results.

The methodology for μQFR has been previously described[28] and is summarized as follows: 1) selection of a single angiographic projection with optimal lesion exposure; 2) delineation of the lumen contours of both the interrogated vessel and major side branches; 3) reconstruction of the reference vessel diameter considering the step-down phenomenon across bifurcations based on the Murray bifurcation fractal law; 4) automatic derivation of TIMI frame count-based contrast flow velocity, which was then converted into hyperemic flow velocity; and 5) calculation of pressure drop based on fluid dynamic equations using the previously mentioned hyperemic flow velocity as a boundary condition. Ultimately, the μQFR pull back along the interrogated vessel was computed, and the μQFR value at the distal end of each side branch was obtained.

Physiologically significant stenosis was identified by pre-PCI μQFR ≤0.80. Based on previous publications reporting the prognostic value of post-PCI wire-based FFR[16] or image-based computational FFR,[19,34] a cutoff of <0.90 was selected a priori for post-PCI μQFR to identify suboptimal physiological outcome post-PCI.

REPRODUCIBILITY OF POST-PCI μQFR. The inter-observer and intraobserver variability of post-PCI μQFR was evaluated in 30 patients randomly selected from the overall population. These patients were reanalyzed by the same analyst 12 months later and by another analyst, following the same standard operation procedure. The analyses were blinded to

FIGURE 1 Study Flowchart



The study flow is presented. A total of 305 vessels randomized to the fractional flow reserve (FFR) arm and 526 vessels randomized to the intravascular ultrasound (IVUS) imaging arm that were managed with percutaneous coronary intervention (PCI) were included from the prospective FLAVOUR trial. Twenty-five vessels were excluded from post-PCI Murray law-based quantitative flow ratio (μQFR) analysis mainly because of lack of final post-PCI angiogram or suboptimal post-PCI image quality. Thus, post-PCI μQFR was successfully analyzed in 806 vessels from 777 patients. The primary endpoint was 2-year target vessel failure defined as a composite of cardiac death, target vessel myocardial infarction, and target vessel revascularization.

clinical outcomes, previous post-PCI μQFR values, post-PCI FFR values (if available), and to each other's results.

STATISTICAL ANALYSIS. Continuous variables were tested for normal distribution by Kolmogorov-Smirnov test, and are reported as mean ± SD if normally distributed or as median (quartiles) if non-normally distributed. Comparisons of continuous variables were performed by Student's *t*-test for normally distributed data, and by Mann-Whitney *U* test for non-normally distributed data. Categorical variables were reported as counts (percentage) and compared using the chi-square or Fisher exact test, as appropriate.

Analyses were performed on a per-vessel level in the intention-to-treat population. Harrel's c-statistic was used to assess the predictive performance of post-PCI μQFR in differentiating 2-year TVF. Kaplan-Meier curves were used to compare 2-year event rates between groups with high and low post-PCI μQFR. The association among demographic, angiographic, procedural variables, and post-PCI μQFR (both as a continuous and dichotomous variable) with 2-year TVF was assessed using HRs with 95% CIs in Cox proportional hazards model, with adjustment for potentially relevant clinical confounders and procedural parameters. Specifically, the multilevel mixed-effects Cox regression model was used to account for center- and patient-level clustering and heterogeneity. The predictive value of post-PCI μQFR <0.90 was further tested in the following predefined interaction (subgroups) analysis: 1) age <65 years vs ≥65 years; 2) women vs men; 3) body mass index <25 kg/m^2 vs ≥25 kg/m^2; 4) left ventricular ejection fraction ≤55% vs >55%; 5) with vs without diabetes mellitus; 6) with vs without hypertension; 7) with vs without hyperlipidemia; 8) with vs without smoking habit; 9) with vs without chronic kidney disease; 10) presence vs absence of acute coronary syndrome; 11) with vs without prior MI; 12) with vs without prior PCI; 13) reference vessel diameter <2.5 mm vs ≥2.5 mm; 14) stent length <30 mm vs ≥30 mm; 15) post-PCI SYNTAX score as 0 vs ≥1; 16) with vs without PCI optimization; and 17) under IVUS vs FFR guidance. In sensitivity analyses, association of post-PCI μQFR and clinical outcomes were further tested in

TABLE 1 Baseline Patient Characteristics

	Overall (N = 777)	FFR Group (n = 283)	IVUS Group (n = 494)	*P* Value[a]
Demographics				
Age, y	65 (58, 72)	64 (58, 71)	65 (58, 73)	0.333
Female	202 (26.0)	64 (22.6)	138 (27.9)	0.104
LVEF, %	64 (59, 69) (n = 674)	64 (58, 69) (n = 236)	64 (60, 69) (n = 438)	0.208
Medical history				
Diabetes mellitus	268 (34.5)	98 (34.6)	170 (34.4)	0.951
Hypertension	541 (69.6)	194 (68.6)	347 (70.2)	0.622
Hypercholesterolemia	632 (81.3)	239 (84.5)	393 (79.6)	0.092
Current smoking	146 (18.8)	56 (19.8)	90 (18.2)	0.590
Chronic kidney disease	148 (19.0)	50 (17.7)	98 (19.8)	0.458
Previous MI	47 (6.0)	22 (7.8)	25 (5.1)	0.127
Clinical presentation				
Chronic coronary syndrome	472 (60.7)	148 (52.3)	324 (65.6)	**0.002**
Acute coronary syndrome	305 (39.3)	135 (47.7)	170 (34.4)	
Baseline SYNTAX score	9 (7, 13)	9 (7, 14)	8 (6, 13)	0.081
Post-PCI SYNTAX score	2 (0, 5)	2 (0, 5)	2 (0, 5)	0.984
Discharge medications				
Aspirin	760 (97.8)	275 (97.2)	485 (98.2)	0.357
$P2Y_{12}$ inhibitor	773 (99.5)	281 (99.3)	492 (99.6)	0.572
DAPT	757 (97.4)	273 (96.5)	484 (98.0)	0.201
Statin	753 (96.9)	278 (98.2)	475 (96.2)	0.107

Values are median (Q1, Q3) or n (%). [a]Test for difference between fractional flow reserve (FFR) and intravascular ultrasound (IVUS) groups has not been adjusted for multiplicity and cannot be used to infer treatment effects.

DAPT = dual antiplatelet therapy; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; SYNTAX = SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery.

the per-protocol population and by using the cutoff derived by maximally selected log-rank statistics. Tests for proportional hazards of each covariate were based on scaled Schoenfeld residuals. In all Cox regression models, the proportional hazards assumption was satisfied.

In FFR-guidance arm, the correlation between pre-PCI μQFR and pre-PCI FFR was evaluated by Spearman's correlation coefficient, while their agreement was tested by Bland-Altman analysis. The non-time dependent area under the receiver-operating characteristic curve was used to evaluate the diagnostic performance of pre-PCI μQFR in predicting pre-PCI FFR ≤0.80. Similar tests were performed for post-PCI μQFR and post-PCI FFR, using <0.90 at cutoff value.

Intraobserver and interobserver agreement for assessing post-PCI μQFR was assessed by Bland-Altman analysis and by means of kappa coefficient.

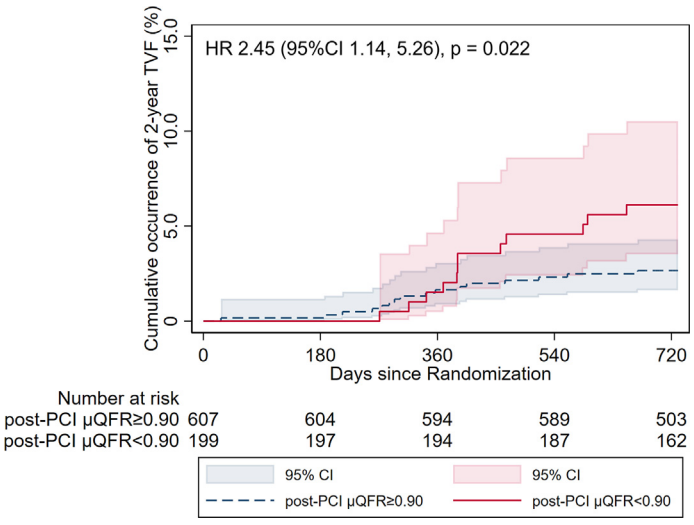
Statistical significance was defined as a 2-tailed *P* value <0.05. The multilevel mixed-effects Cox regression was performed using the coxme package in R 4.4.1 (R Foundation for Statistical Computing). Other statistical analyses were performed with SPSS version 25 (SPSS, Inc) and Stata version 16.0 (StataCorp).

RESULTS

BASELINE CLINICAL AND LESION CHARACTERISTICS. In the FLAVOUR trial population, 901 vessels were randomized to IVUS imaging arm and 919 vessels to FFR arm. More vessels were managed with PCI in IVUS group (58.4%, 526 of 901) compared with the FFR group (33.2%, 305 of 919; $P < 0.0001$) (Figure 1). A total of 25 vessels were excluded from post-PCI μQFR analysis mainly because of lack of final post-PCI angiogram or suboptimal post-PCI image quality. Therefore, post-PCI μQFR was successfully analyzed in 806 vessels from 777 patients, resulting in an overall vessel-level feasibility of 97.0% (806 of 831). In the FFR guidance group, pre-PCI μQFR was successfully analyzed in 877 of 919 vessels (feasibility 95.4%).

Median age was 65 years (Q1-Q3: 58-72 years), 26.0% (202 of 777) were women, and 34.5% (268 of 777) had diabetes mellitus (Table 1). At a vessel level, 63.6% (513 of 806) were left anterior descending artery (Supplemental Table 1). Vessels undergoing IVUS-guided stenting had milder percent diameter stenosis (DS%), shorter lesions, and higher pre-PCI μQFR at baseline (Supplemental Table 1). Median post-PCI μQFR was 0.93 (Q1-Q3: 0.90-0.96). Post-PCI μQFR was <0.90 in 24.7% (199 of 806) of the

FIGURE 2 Cumulative Occurrence of 2-Year TVF Stratified by Post-PCI μQFR <0.90



Kaplan-Meier curve is presented for cumulative occurrence of target vessel failure (TVF) at 2 years between the post-PCI μQFR <0.90 group and the post-PCI μQFR ≥0.90 group in the overall population. Multilevel mixed-effects Cox proportional hazards regression was used to calculate the crude HRs and 95% CIs. It shows that vessels with post-PCI μQFR values <0.90 had significantly higher 2-year TVF rate compared with those with values ≥0.90 (6.1% [12 of 199] vs 2.7% [16 of 607]; HR: 2.45 [95% CI: 1.14-5.26]; $P = 0.022$). Please note that the curves are starting to diverge after 1 year. Abbreviations as in Figure 1.

vessels, and ≤0.80 in 2.7% (22 of 806) (Supplemental Figure 2).

DIAGNOSTIC ACCURACY OF μQFR IN THE FFR-GUIDANCE GROUP. Median was 0.88 (Q1-Q3: 0.79-0.93) for pre-PCI μQFR and 0.85 (Q1-Q3: 0.78-0.90) for pre-PCI FFR. Pre-PCI μQFR ≤0.80 and pre-PCI FFR ≤0.80 was identified in 30.6% (268 of 877) and 32.5% (285 of 877) vessels, respectively. Pre-PCI μQFR showed good correlation (r = 0.73 [95% CI: 0.69-0.76]; $P < 0.0001$) with pre-PCI FFR (Supplemental Figure 3). Using an FFR ≤0.80 for identifying physiologically significant stenosis, the vessel-level accuracy of pre-PCI μQFR ≤0.80 was 90% (95% CI: 88%-92%), with a sensitivity of 82% (95% CI: 77%-86%) and a specificity of 94% (95% CI: 92%-96%) (Supplemental Table 2). The AUC for pre-PCI μQFR in predicting FFR ≤0.80 was 0.95 (95% CI: 0.93-0.96); $P < 0.0001$ (Supplemental Figure 4).

Paired post-PCI FFR and μQFR was available in 262 vessels. Post-PCI μQFR showed moderate correlation (r = 0.44 [95% CI: 0.33-0.53]; $P < 0.0001$) and diagnostic concordance with post-PCI FFR (AUC: 0.73 [95% CI: 0.67-0.78], accuracy 61% [95% CI: 56%-67%], both using <0.90 as cutoff) (Supplemental Figures 5 and 6, Supplemental Tables 3 and 4).

PROGNOSTIC VALUE OF POST-PCI μQFR IN THE OVERALL POPULATION. Complete 2-year follow-up data were available for 99.3% (800 of 806) of the treated vessels and a total of 28 (3.5%) TVF were detected. The rate of TVF decreased with increasing ranges of post-PCI μQFR (Supplemental Figure 7). Vessels with 2-year TVF had lower post-PCI μQFR values (0.90 ± 0.05) compared with those without (0.92 ± 0.05; $P = 0.042$). Vessels with post-PCI μQFR values <0.90 had a significantly higher 2-year TVF rate compared with those with values ≥0.90 (6.1% [12 of 199] vs 2.7% [16 of 607]; HR: 2.45 [95% CI: 1.14-5.26]; $P = 0.022$) (**Figure 2**, **Table 2**). The trend was similar in per-protocol population (Supplemental Table 5). Other variables, including multivessel disease (HR: 2.91 [95% CI: 1.10-7.66]; $P = 0.031$) and baseline DS% by quantitative coronary angiography (HR: 1.06 [95% CI: 1.01-1.10]; $P = 0.014$) were also independent predictors of 2-year TVF (Supplemental Table 6). The predictive value of post-PCI μQFR <0.90 remained after multivariable adjustment (Supplemental Table 7) and was consistent across subgroups, except for the randomization arms, with post-PCI μQFR <0.90 being more predictive in the IVUS-guided group than in the FFR-guided group (**Figure 3**).

The Harrel's c-statistic was 0.54 (95% CI: 0.46-0.61) for post-PCI μQFR in differentiating 2-year TVF. By using the maximally selected log-rank test, a cutoff of ≤0.93 was identified for post-PCI μQFR as having the best predictive accuracy for 2-year TVF. Post-PCI μQFR ≤0.93 showed similar prognostic value for predicting 2-year TVF (4.9% [22 of 449] vs 1.7% [6 of 357]; HR: 3.24 [95% CI: 1.30-8.09]; $P = 0.012$) (Supplemental Table 8).

In the FFR-guidance group, neither post-PCI FFR (per 0.10 increase: HR: 0.75 [95% CI: 0.26-2.13]; $P = 0.585$) nor post-PCI FFR <0.90 (3.7% [6 of 163] vs 4.0% [4 of 99], HR: 0.90 [95% CI: 0.26-3.21];

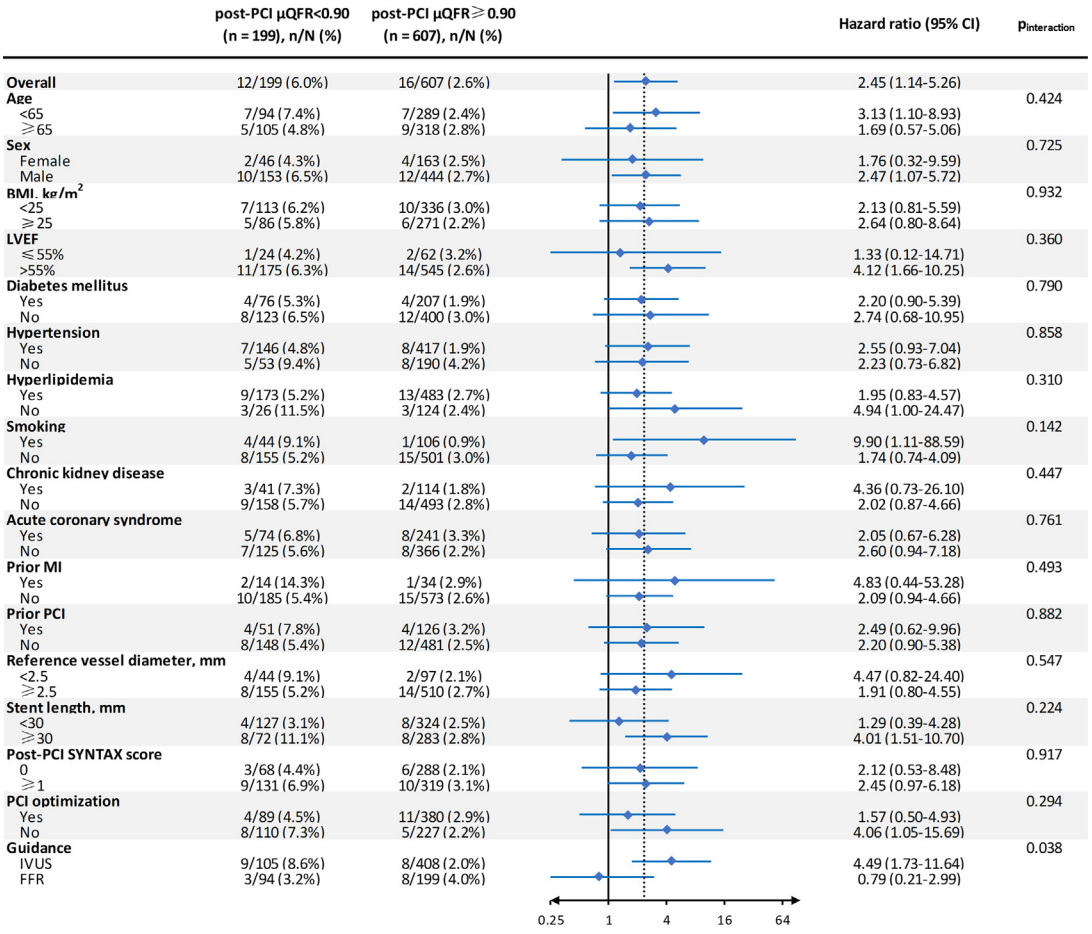
TABLE 2 Events at 2-Year Stratified by Post-PCI μQFR <0.90 in Overall Population[a]

	Post-PCI μQFR <0.90 (n = 199)	Post-PCI μQFR ≥0.90 (n = 607)	HR (95% CI)	*P* Value
TVF	12 (6.1)	16 (2.7)	2.45 (1.14-5.26)	**0.022**
Cardiac death	4 (2.0)	2 (0.3)	6.14 (1.12-33.52)	**0.036**
TVMI	0 (0.0)	3 (0.5)	–	–
TVR	8 (4.1)	13 (2.2)	2.10 (0.85-5.17)	0.110
Cardiac death or TVMI	4 (2.0)	5 (0.8)	2.16 (0.56-8.28)	0.260

Values are n (%) unless otherwise indicated. [a]Complete 2-year follow-up was available in 99.3% (800 of 806) of the vessels.

μQFR = Murray law-based quantitative flow ratio; PCI = percutaneous coronary intervention; TVMI = target vessel myocardial infarction; TVF = target vessel failure; TVR = target vessel revascularization.

FIGURE 3 Subgroup Analyses for Post-PCI μQFR in Predicting 2-Year TVF



Subgroup analyses are presented for post-PCI μQFR in predicting 2-year TVF. The incidences of 2-year TVF (%) were listed and compared between the post-PCI μQFR <0.90 and ≥0.90 groups. Cox proportional hazards regression was used to calculate the crude HRs and 95% CIs. *P* for interaction <0.05 indicated statistical significance. It showed that the prognostic value of post-PCI μQFR <0.90 in predicting 2-year TVF rate was consistent across subgroups except for the randomization arms, with post-PCI μQFR <0.90 more predictive in IVUS than in FFR group. BMI = body mass index; LVEF = left ventricular ejection fraction; MI = myocardial infarction; SYNTAX = SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery; other abbreviations as in Figure 1.

$P = 0.877$) was associated with 2-year TVF. Post-PCI FFR showed a similar Harrel's c-statistic compared with post-PCI μQFR for predicting 2-year TVF (0.51 [95% CI: 0.36-0.67] vs 0.51 [95% CI: 0.37-0.66]; $P = 0.99$).

REPRODUCIBILITY OF POST-PCI μQFR. Repeated post-PCI μQFR analysis was performed in 30 vessels from 30 patients. The interobserver and intraobserver variability in post-PCI μQFR was 0.00 ± 0.04 and 0.00 ± 0.03, respectively. The kappa coefficient was 0.66 (95% CI: 0.55-0.76) within the same observer and 0.61 (95% CI: 0.44-0.78) between 2 independent observers.

DISCUSSION

To our knowledge, this is the first study to evaluate the potential role of μQFR, a novel method for fast computation of FFR from a single angiographic projection, in predicting clinical outcomes when assessed immediately after successful PCI under systematic

FFR or IVUS guidance (**Central Illustration**). The key findings of our study can be summarized as follows:

1. The assessment of μQFR from a single angiographic view was highly feasible, both before PCI (95.4%, 877 of 919 vessels) and immediately after successful PCI (97.0%, 806 of 831 vessels).
2. Pre-PCI μQFR demonstrated high diagnostic concordance with wire-based FFR, whereas post-PCI μQFR correlated to a lesser extent with post-PCI FFR.
3. Despite undergoing FFR- or IVUS-guided successful PCI, approximately one-fourth of the vessels presented with suboptimal physiological outcome post-PCI as evaluated by post-PCI μQFR <0.90.
4. Post-PCI μQFR was an independent predictor of 2-year TVF, the predictive value was significant in IVUS-guided group but not in FFR-guided group.

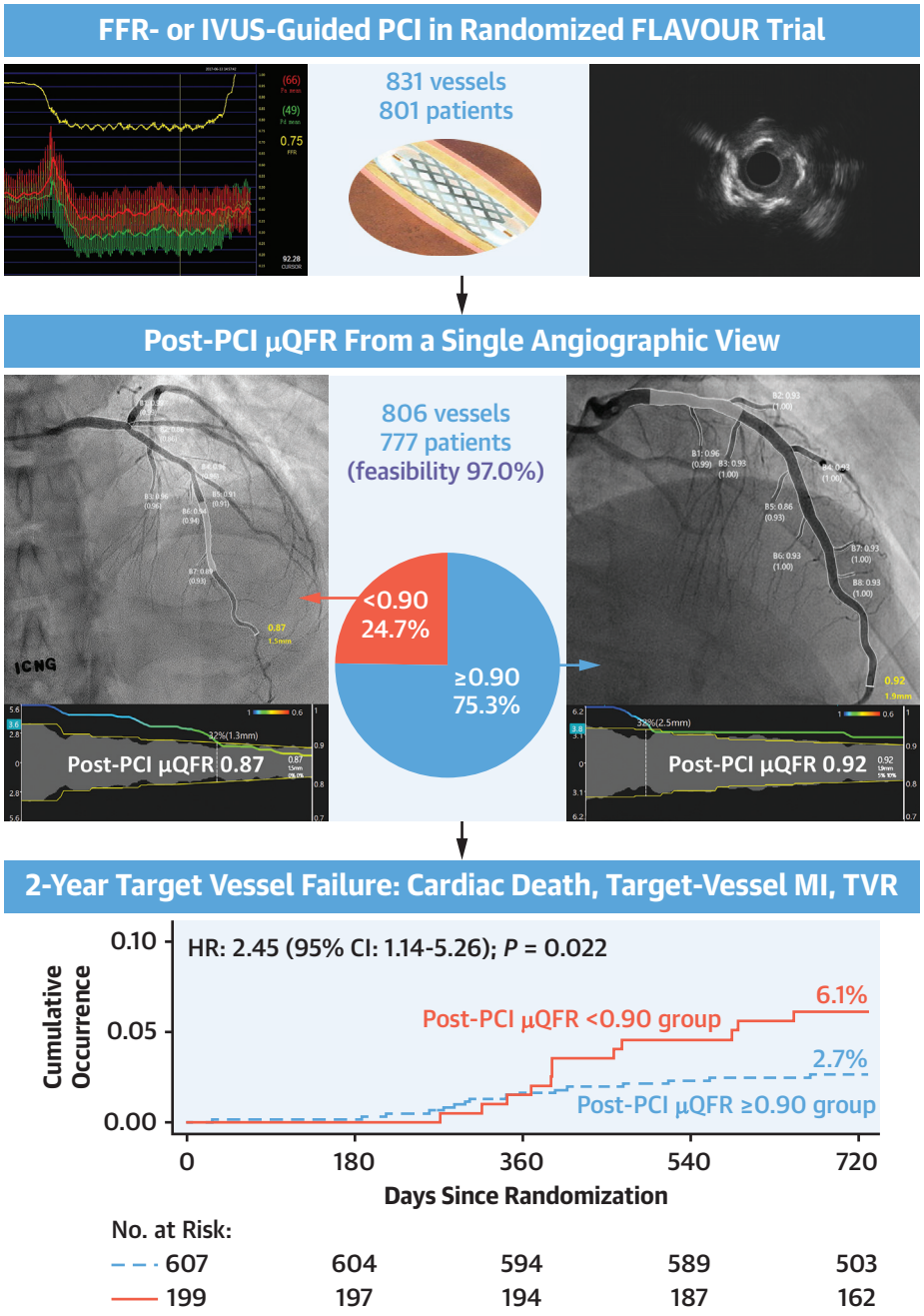
The association of post-PCI μQFR with clinical outcomes aligns with existing evidence showing the prognostic value of post-PCI wire-based physiological assessments.[7-20,35-42] Currently, the clinical adoption of wire-based physiology remains limited, especially after PCI, because of the inherent limitations of pressure wire-based measurements and operators' confidence in relying on visual assessment alone.[21] Computational FFR techniques have recently emerged as alternatives that eliminate the need for costly pressure wires or hyperemia-inducing medications.[43] Several commercially available techniques of angiography-based computational FFR, including QFR, vFFR, and FFRangio, showed good diagnostic concordance with invasive wire-based FFR.[44] Among these techniques, QFR[19,20,24-27] and vFFR[45] have demonstrated association with clinical outcomes in post-PCI settings in several pilot studies. The prospective HAWKEYE study showed that post-PCI QFR ≤0.89 was associated with a 3-fold increase in risk of vessel-oriented composite endpoint at 2 years.[19] Similar results were found in patients with 3-vessel disease[20] or ST-segment elevation MI[24] undergoing DES implantation. The FAST Outcome study consistently showed that lower post-PCI vFFR were associated with increased risk of 5-year TVF and TVR.[45] In these studies, the analyzability of traditional angiography-based FFR techniques ranged from 42% to 85% post-PCI,[19,20,24-27,45] mostly because of insufficient angle separation for reliable 3D reconstruction, excessive vessel overlap or tortuosity at the stenotic segments, or with only one angiographic projection available post-PCI.

Recently, a pilot study investigating single-view μQFR after PCI proved that residual ischemia identified by μQFR after left main bifurcation stenting was associated with higher risk of 3-year cardiovascular death.[46] In our study, the prognostic value of post-PCI μQFR extended to intermediate angiographic lesions, treated under systematic guidance of physiology or intravascular imaging. Of note, unlike traditional angiography-based FFR that relies on 2 or more angiographic views, the feasibility of post-PCI μQFR from a single angiographic view was 94% in a previous study[46] and 97% in current analysis. The fact that physiological evaluation can be timely obtained through a single conventional angiography is fascinating. It may facilitate physiology-guided PCI procedures in accordance with guideline recommendations,[47] especially in emerging countries where systematic physiological assessments are not readily affordable or available.[48]

Our data additionally provided validation of pre-PCI μQFR against wire-based FFR using a large-scale prospective RCT data set, corroborating previous pilot validation studies.[29,30] In comparison, the post-PCI μQFR correlated to a lesser extent with post-PCI FFR, possibly secondary to the following reasons. In post-PCI data sets, μQFR and FFR show high median values and relatively narrow distribution, which can make a strong correlation difficult to achieve. Because angiography is insensitive to detecting intrastent abnormalities including stent malapposition and underexpansion, in-stent pressure loss, if present, might have been underestimated by angiography-based μQFR,[49] thus resulting in higher post-PCI μQFR values compared with FFR. Of note, our results showed that the prognostic relevance of post-PCI μQFR could not be excluded despite the lack of adequate correlation with invasive post-PCI FFR.

Interestingly, the predictive value of post-PCI μQFR was more significant in vessels undergoing PCI and optimization guided by IVUS (HR: 4.49 [95% CI: 1.73-11.64]) compared with FFR-guided cases (HR: 0.79 [95% CI: 0.21-2.99]). We also found that final post-PCI FFR was not predictive of 2-year TVF in patients randomized to receive stenting and PCI optimization as needed, under systematic FFR guidance. This lack of statistical significance is possibly caused by small number of events (10 TVFs) observed in the FFR-guidance PCI arm. In addition, unlike previous observational studies, in which systematic physiological guidance was rarely used,[16] suboptimal stenting results in FLAVOUR patients from the FFR-guidance arm were corrected; thus, post-PCI physiology might not be the predominant factor in causing future adverse events. In this case, residual risk might predominantly result from stent-related abnormalities or vulnerable plaque, none of which can be detected by the angiogram. By comparison, in the

CENTRAL ILLUSTRATION **Prognostic Value of Post-PCI μQFR From a Single Angiographic View**



Ding D, et al. JACC Asia. 2025;5(1):59-70.

Patients enrolled in the FLAVOUR (Fractional FLow Reserve And IVUS for Clinical OUtcomes in Patients With InteRmediate Stenosis) trial (NCT02673424) randomized to receive either fractional flow reserve (FFR) or intravascular ultrasound (IVUS)-guided stenting by second-generation drug-eluting stents were included. Postpercutaneous coronary intervention (PCI) Murray-law based quantitative flow ratio (μQFR) was successfully analyzed from a single angiographic view acquired immediately after PCI in 806 of 831 treated vessels, with a feasibility of 97.0%. Physiological outcome post-PCI was suboptimal (post-PCI μQFR <0.90) in 24.7% (199 of 806) of vessels, despite FFR- or IVUS-guided PCI. Vessels with post-PCI μQFR values <0.90 had a significantly higher rate of 2-year target vessel failure defined as a composite of cardiac death, target-vessel myocardial infarction (MI), and target vessel revascularization (TVR), compared with those with values ≥0.90 (6.1% [12 of 199] vs 2.7% [16 of 607]; HR: 2.45 [95% CI: 1.14-5.26]; $P = 0.022$).

IVUS-guidance arm, post-PCI μQFR independently provides prognostic value. These findings prompt the hypothesis that the combined use of intracoronary imaging and image-based physiology could reveal how and why suboptimal stenting may adversely affect patient outcomes but warrant further investigation.

The high prevalence (24.7%, 199 of 806 vessels) of suboptimal post-PCI μQFR, despite FFR- or IVUS-guided PCI, aligns with recent clinical trials or registries.[34] Specifically, the rate of post-PCI μQFR <0.90 was higher in the FFR group compared with the IVUS group (32.1% [94 of 293 vessels] vs 20.5% [105 of 513 vessels]), partially because of the fact that severer lesions had been included in the FFR vs IVUS group. The TARGET-FFR (Trial of Angiography vs. pressure-Ratio-Guided Enhancement Techniques -Fractional Flow Reserve) trial showed the difficulty in achieving post-PCI FFR >0.90, even with systematic FFR-guided PCI optimization.[10] In the FFR-REACT (FFR-Guided PCI Optimization Directed by High-Definition IVUS Versus Standard of Care) trial, systematic IVUS-guided PCI optimization resulted in significant but small improvement in post-PCI physiology, with final post-PCI FFR <0.90 still present in 80% of the vessels.[50] Correcting a suboptimal post-PCI result to achieve higher post-PCI physiology might have limited efficacy, and whether this improvement translates into clinical benefit is still under investigation. Consequently, there is growing interest in preventing suboptimal PCI results before stent implantation. In this regard, image-based computational FFR from pre-PCI images with virtual stenting has been developed and validated, showing good correlation and agreement with actual post-PCI physiology.[26,49,51-53] The recent randomized AQVA (Angio-based Quantitative Flow Ratio Virtual PCI Versus Conventional Angio-guided PCI in the Achievement of an Optimal Post-PCI QFR) trial demonstrated the superiority of QFR-based virtual PCI over angiography-based PCI in achieving optimal post-PCI physiological results.[54] The randomized AQVA II (Angio- or Microcatheter-Quantified FFR Virtual PCI Versus Angio-Guided PCI in the Achievement of an Optimal Post-PCI FFR) trial focusing on complex and high-risk procedures further showed that procedural planning and guidance based on single-view μQFR was noninferior to FFR guidance.[55] Given the high feasibility and availability, μQFR based on a single angiographic view might be a promising tool for PCI planning, which needs to be tested in future randomized studies.

STUDY LIMITATIONS. All analyses were performed post hoc and off-line in an independent academic core laboratory. We have made sure that all the μQFR analyses were performed strictly blinded to any clinical outcomes and/or FFR data. In addition, the observed high overall feasibility of μQFR might have been facilitated by the fact that all coronary angiographies, collected within the framework of a study, were conducted in the setting of a prospective trial. It is important to investigate the reproducibility of our findings in a real-life scenario, where online assessment is performed.

The association of post-PCI μQFR and clinical outcomes was evaluated at a vessel level instead of a patient level. Because patient-level outcomes are driven by both target and nontarget lesions/vessels, total physiologic atherosclerotic burden assessed by sum of μQFR in 3 major epicardial vessels (ie, 3V-μQFR) would be needed for such analysis.[56-59] However, because our study is a post hoc analysis based on the prospective FLAVOUR trial, angiograms acquired in optimal projections were not always available for nontarget vessels, and thus, a reliable 3V-μQFR analysis was not enabled.

The location of the FFR pressure wire was not always recorded for comparison with μQFR, neither pre- nor post-PCI. This may introduce variability in the location for FFR-μQFR comparison and could potentially impact the numerical agreement of μQFR and FFR, especially in the presence of residual or diffuse disease.

The role of post-PCI μQFR directly compared with post-PCI FFR in predicting patient outcomes warrants further investigation in larger populations with higher incidence of adverse events. Because post-PCI μQFR and post-PCI FFR values may not always align, the impact of concordant or discordant post-PCI μQFR/FFR groups on clinical prognosis is worth investigating.

Finally, the generalizability of our findings to populations without systematic physiology or intracoronary imaging-guidance remains unknown. The study population was limited to patients enrolled in the current trial, and therefore, caution should be exercised when extrapolating the results to broader patient cohorts without similar guidance strategies.

CONCLUSIONS

In patients with intermediate lesions who underwent PCI with contemporary imaging or physiology guidance, lower post-PCI μQFR values predict subsequent

adverse events. The high feasibility, accuracy, and independent prognostic value of μQFR make it a promising tool for optimizing PCI outcomes.

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REFERENCES

1. Abdallah MS, Wang K, Magnuson EA, et al. Quality of life after PCI vs CABG among patients with diabetes and multivessel coronary artery disease: a randomized clinical trial. *J Am Med Assoc*. 2013;310:1581–1590.

2. Tonino PAL, De Bruyne B, Pijls NHJ, et al, FAME Study Investigators. Fractional flow reserve vs angiography for guiding percutaneous coronary intervention. *N Engl J Med*. 2009;360:213–224.

3. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med*. 2007;356:1503–1516.

4. Pijls NH, van Schaardenburgh P, Manoharan G, 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.

5. Collet C, Collison D, Mizukami T, et al. Differential improvement in angina and health-related quality of life after PCI in focal and diffuse coronary artery disease. *JACC Cardiovasc Interv*. 2022;15:2506–2518.

6. Stone GW, Kereiakes DJ, Gori T, et al. 5-year outcomes after bioresorbable coronary scaffolds implanted with improved technique. *J Am Coll Cardiol*. 2023;82:183–195.

7. Jeremias A, Davies JE, Maehara A, et al. Blinded physiological assessment of residual ischemia after successful angiographic percutaneous coronary intervention: the DEFINE PCI study. *JACC Cardiovasc Interv*. 2019;12:1991–2001.

8. van Bommel RJ, Masdjedi K, Diletti R, et al. Routine fractional flow reserve measurement after percutaneous coronary intervention - The FFR-SEARCH study. *Circ Cardiovasc Interv*. 2019;12:e007428.

9. 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;9:1022–1031.

10. Collison D, Didagelos M, Aetesam-Ur-Rahman M, et al. Post-stenting fractional flow reserve vs coronary angiography for optimization of percutaneous coronary intervention (TARGET-FFR). *Eur Heart J*. 2021;42:4656–4668.

11. Piroth Z, Toth GG, Tonino PAL, et al. Prognostic value of fractional flow reserve measured immediately after drug-eluting stent implantation. *Circ Cardiovasc Interv*. 2017;10:e005233.

12. Hanekamp CE, Koolen JJ, Pijls NH, Michels HR, Bonnier HJ. Comparison of quantitative coronary angiography, intravascular ultrasound, and coronary pressure measurement to assess optimum stent deployment. *Circulation*. 1999;99:1015–1021.

13. Bech GJW, Pijls NHJ, De Bruyne B, et al. Usefulness of fractional flow reserve to predict clinical outcome after balloon angioplasty. *Circulation*. 1999;99:883–888.

14. Fearon WF, Luna J, Samady H, et al. Fractional flow reserve compared with intravascular ultrasound guidance for optimizing stent deployment. *Circulation*. 2001;104:1917–1922.

15. Johnson NP, Tóth GG, Lai D, et al. Prognostic value of fractional flow reserve: linking physiologic severity to clinical outcomes. *J Am Coll Cardiol*. 2014;64:1641–1654.

16. Rimac G, Fearon WF, De Bruyne B, et al. Clinical value of post-percutaneous coronary intervention fractional flow reserve value: a systematic review and meta-analysis. *Am Heart J*. 2017;183:1–9.

17. 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;11:2099–2109.

18. Hakeem A, Uretsky BF. Role of post-intervention fractional flow reserve to improve procedural and clinical outcomes. *Circulation*. 2019;139:694–706.

19. Biscaglia S, Tebaldi M, Brugaletta S, et al. Prognostic value of QFR measured immediately after successful stent implantation: the international multicenter prospective HAWKEYE study. *JACC Cardiovasc Interv*. 2019;12:2079–2088.

20. Kogame N, Takahashi K, Tomaniak M, et al. Clinical implication of quantitative flow ratio after percutaneous coronary intervention for 3-vessel disease. *JACC Cardiovasc Interv*. 2019;12:2064–2075.

21. Tebaldi M, Biscaglia S, Fineschi M, et al. Evolving routine standards in invasive hemodynamic assessment of coronary stenosis: The nationwide Italian SICI-GISE cross-sectional ERIS study. *JACC Cardiovasc Interv*. 2018;11:1482–1491.

22. 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;9:2024–2035.

23. Xu B, Tu S, Song L, et al. Angiographic quantitative flow ratio-guided coronary intervention (FAVOR III China): a multicentre, randomised, sham-controlled trial. *Lancet*. 2021;398:2149–2159.

24. Tang J, Chu J, Hou H, et al. Clinical implication of QFR in patients with ST-segment elevation myocardial infarction after drug-eluting stent implantation. *Int J Cardiovasc Imaging*. 2021;37:755–766.

25. Erbay A, Penzel L, Abdelwahed YS, et al. Feasibility and diagnostic reliability of quantitative flow ratio in the assessment of non-culprit lesions in acute coronary syndrome. *Int J Cardiovasc Imaging*. 2021;37:1815–1823.

26. Zhang R, Xu B, Dou K, et al. Post-PCI outcomes predicted by pre-intervention simulation of residual quantitative flow ratio using augmented reality. *Int J Cardiol*. 2022;352:33–39.

27. Saito Y, Cristea E, Bouras G, et al. Long-term serial functional evaluation after implantation of the Fantom sirolimus-eluting bioresorbable coronary scaffold. *Catheter Cardiovasc Interv*. 2021;97:431–436.

28. Tu S, Ding D, Chang Y, Li C, Wijns W, Xu B. Diagnostic accuracy of quantitative flow ratio for assessment of coronary stenosis significance from a single angiographic view: a novel method based on bifurcation fractal law. *Catheter Cardiovas Interv*. 2021;97:1040–1047.

29. Ding D, Tu S, Chang Y, Li C, Xu B, Wijns W. Quantitative flow ratio based on Murray fractal law: accuracy of single vs two angiographic views. *J Soc Cardiovasc Angiogr Interv*. 2022;1:100399.

30. Cortés C, Liu L, Berdin SL, et al. Agreement between Murray law-based quantitative flow ratio (μQFR) and three-dimensional quantitative flow ratio (3D-QFR) in non-selected angiographic stenosis: a multicenter study. *Cardiol J*. 2022;29:388–395.

31. Kang J, Koo BK, Hu X, et al. Comparison of fractional flow reserve and intravascular ultrasound-guided intervention strategy for clinical outcomes in patients with intermediate stenosis (FLAVOUR). *Am Heart J*. 2018;199:7–12.

32. Koo BK, Hu X, Kang J, et al. Fractional flow reserve or intravascular ultrasonography to guide PCI. *N Engl J Med*. 2022;387:779–789.

33. Garcia-Garcia HM, McFadden EP, Farb A, et al. Standardized end point definitions for coronary intervention trials: The Academic Research Consortium-2 consensus document. *Circulation*. 2018;137:2635–2650.

34. Ding D, Huang J, Westra J, et al. Immediate post-procedural functional assessment of percutaneous coronary intervention: current evidence and future directions. *Eur Heart J*. 2021;42:2695–2707.

35. Hwang D, Koo BK, Zhang J, et al. Prognostic implications of fractional flow reserve after coronary stenting: a systematic review and meta-analysis. *JAMA Netw Open*. 2022;5:e2232842.

36. Andersen BK, Ding D, Mogensen LJH, et al. Predictive value of post-percutaneous coronary intervention fractional flow reserve: a systematic review and meta-analysis. *Eur Heart J Qual Care Clin Outcomes*. 2022;9:99–108.

37. Wolfrum M, Fahrni G, de Maria GL, et al. Impact of impaired fractional flow reserve after coronary interventions on outcomes: a systematic review and meta-analysis. *BMC Cardiovasc Disord*. 2016;16:177.

38. Griffioen AM, van den Oord SCH, Teerenstra S, Damman P, van Royen N, van Geuns RJM. Clinical relevance of impaired physiological assessment after percutaneous coronary intervention: a meta-analysis. *J Soc Cardiovasc Angiogr Interv*. 2022;1:100448.

39. Patel MR, Jeremias A, Maehara A, et al. 1-year outcomes of blinded physiological assessment of residual ischemia after successful PCI: DEFINE PCI trial. *JACC Cardiovasc Interv*. 2022;15:52–61.

40. Hakeem A, Ghosh B, Shah K, et al. Incremental prognostic value of post-intervention Pd/Pa in patients undergoing ischemia-driven percutaneous coronary intervention. *JACC Cardiovasc Interv*. 2019;12:2002–2014.

41. Shin D, Lee SH, Lee JM, et al. Prognostic implications of post-intervention resting Pd/Pa and fractional flow reserve in patients with stent implantation. *JACC Cardiovasc Interv*. 2020;13:1920–1933.

42. Collet C, Johnson NP, Mizukami T, et al. Impact of post-PCI FFR stratified by coronary artery. *JACC Cardiovasc Interv*. 2023;16:2396–2408.

43. Tu S, Westra J, Adjedj J, et al. Fractional flow reserve in clinical practice: from wire-based invasive measurement to image-based computation. *Eur Heart J*. 2020;41:3271–3279.

44. Collet C, Onuma Y, Sonck J, et al. Diagnostic performance of angiography-derived fractional flow reserve: a systematic review and Bayesian meta-analysis. *Eur Heart J*. 2018;39:3314–3321.

45. Neleman T, Scoccia A, Masdjedi K, et al. The prognostic value of angiography-based vessel fractional flow reserve after percutaneous coronary intervention: The FAST Outcome study. *Int J Cardiol*. 2022;359:14–19.

46. Wang HY, Zhang R, Dou K, et al. Left main bifurcation stenting: impact of residual ischaemia on cardiovascular mortality. *Eur Heart J*. 2023;44(41):4324–4336.

47. Vrints C, Andreotti F, Koskinas KC, et al. 2024 ESC guidelines for the management of chronic coronary syndromes. *Eur Heart J*. 2024;45:3415–3537.

48. Gotberg M, Cook CM, Sen S, Nijjer S, Escaned J, Davies JE. The evolving future of instantaneous wave-free ratio and fractional flow reserve. *J Am Coll Cardiol*. 2017;70:1379–1402.

49. Rubimbura V, Guillon B, Fournier S, et al. Quantitative flow ratio virtual stenting and post stenting correlations to post stenting fractional flow reserve measurements from the DOCTORS (Does Optical Coherence Tomography Optimize Results of Stenting) study population. *Catheter Cardiovasc Interv*. 2020;96:1145–1153.

50. Neleman T, van Zandvoort LJC, Tovar Forero MN, et al. FFR-guided PCI optimization directed by high-definition IVUS vs standard of care: the FFR REACT Trial. *JACC Cardiovasc Interv*. 2022;15:1595–1607.

51. Gosling RC, Morris PD, Silva Soto DA, Lawford PV, Hose DR, Gunn JP. Virtual coronary intervention: a treatment planning tool based upon the angiogram. *JACC Cardiovascular Imaging*. 2019;12:865–872.

52. Gosling RC, Adam Z, Barmby DS, et al. The impact of virtual fractional flow reserve and virtual coronary intervention on treatment decisions in the cardiac catheter laboratory. *Can J Cardiol*. 2021;37:1530–1538.

53. Tomaniak M, Neleman T, Ziedses des Plantes A, et al. Diagnostic accuracy of coronary angiography-based vessel fractional flow reserve (vFFR) virtual stenting. *J Clin Med*. 2022;11:1397.

54. Biscaglia S, Verardi FM, Tebaldi M, et al. QFR-based virtual PCI or conventional angiography to guide PCI: the AQVA trial. *JACC Cardiovasc Interv*. 2023;16:783–794.

55. Biscaglia S, Verardi FM, Erriquez A, et al. Coronary Physiology Guidance vs Conventional Angiography for Optimization of Percutaneous Coronary Intervention: the AQVA II Trial. *JACC Cardiovasc Interv*. 2024;17(2):277–287.

56. Hamaya R, Hoshino M, Kanno Y, et al. Prognostic implication of three-vessel contrast-flow quantitative flow ratio in patients with stable coronary artery disease. *EuroIntervention*. 2019;15:180–188.

57. Fournier S, Collet C, Xaplanteris P, et al. Global fractional flow reserve value predicts 5-year outcomes in patients with coronary atherosclerosis but without ischemia. *J Am Heart Assoc*. 2020;9:e017729.

58. Lee JM, Koo B-K, Shin E-S, et al. Clinical implications of three-vessel fractional flow reserve measurement in patients with coronary artery disease. *Eur Heart J*. 2018;39:945–951.

59. Seike F, Mintz GS, Matsumura M, et al. Impact of intravascular ultrasound–derived lesion-specific virtual fractional flow reserve predicts 3-year outcomes of untreated nonculprit lesions: the PROSPECT study. *Circ Cardiovasc Interv*. 2022;15:851–860.

KEY WORDS angiography-based physiology, clinical outcome, fractional flow reserve, intravascular ultrasound, percutaneous coronary intervention, quantitative flow ratio, second-generation drug-eluting stent(s)

APPENDIX For supplemental Methods, figures, and tables, please see the online version of this paper.