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ORIGINAL PAPER

Characterization of quantitative flow ratio and fractional flow reserve discordance using doppler flow and clinical follow-up

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Abstract

The physiological mechanisms of quantitative flow ratio and fractional flow reserve disagreement are not fully understood. We aimed to characterize the coronary flow and resistance profile of intermediate stenosed epicardial coronary arteries with concordant and discordant FFR and QFR. Post-hoc analysis of the DEFINE-FLOW study. Anatomical and Doppler-derived physiological parameters were compared for lesions with FFR+QFR− (n = 18) vs. FFR+QFR+ (n = 43) and for FFR−QFR+ (n = 34) vs. FFR−QFR− (n = 139). The association of QFR results with the two-year rate of target vessel failure was assessed in the proportion of vessels (n = 195) that did not undergo revascularization. Coronary flow reserve was higher [2.3 (IQR: 2.1–2.7) vs. 1.9 (IQR: 1.5–2.4)], hyperemic microvascular resistance lower [1.72 (IQR: 1.48–2.31) vs. 2.26 (IQR: 1.79–2.87)] and anatomical lesion severity less severe [% diameter stenosis 45.5 (IQR: 41.5–52.5) vs. 58.5 (IQR: 53.1–64.0)] for FFR+QFR− lesions compared with FFR+QFR+ lesions. In comparison of FFR−QFR+ vs. FFR-QFR- lesions, lesion severity was more severe [% diameter stenosis 55.2 (IQR: 51.7–61.3) vs. 43.4 (IQR: 35.0–50.6)] while coronary flow reserve [2.2 (IQR: 1.9–2.9) vs. 2.2 (IQR: 1.9–2.6)] and hyperemic microvascular resistance [2.34 (IQR: 1.85–2.81) vs. 2.57 (IQR: 2.01–3.22)] did not differ. The agreement and diagnostic performance of FFR using hyperemic stenosis resistance (> 0.80) as reference standard was higher compared with QFR and coronary flow reserve. Disagreement between FFR and QFR is partly explained by physiological and anatomical factors.
Clinical Trials Registration https://www.clinicaltrials.gov; Unique identifier: NCT01813435.

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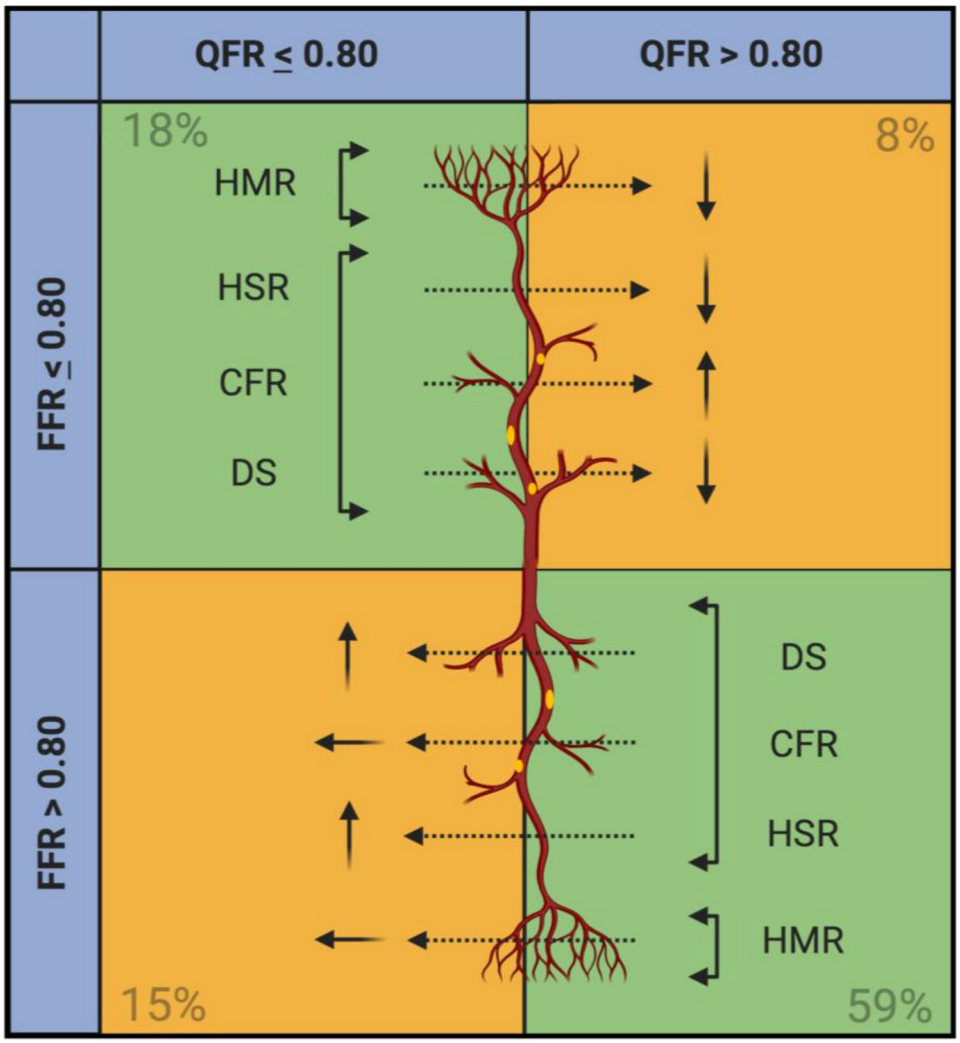
Graphical abstract

Changes in central physiological and anatomical parameters according to FFR and QFR match/mismatch quadrants.



Keywords Fractional flow reserve · Coronary physiology · Coronary flow reserve · Quantitative coronary angiography

Introduction

Physiological lesion assessment is increasingly used for appropriate identification of intermediate coronary artery stenoses suitable for percutaneous coronary intervention (PCI) or bypass surgery [1]. Fractional flow reserve (FFR) guided PCI reduces the rate of spontaneous myocardial infarction and urgent revascularization compared to angiography-guided PCI and/or medical therapy alone [2–4].

Quantitative flow ratio (QFR) based on computation of invasive coronary angiography was recently developed to further expand and improve the use of functional lesion assessment during invasive coronary angiography [5, 6]. For treat/no-treat decisions, QFR and FFR disagree in up to approximately 20% of paired measurements [7]. Previous studies found that the disagreement may be related to microvascular dysfunction, anatomical stenosis characteristics, or the presence of severe aortic valve stenosis [7–11].

To expand our current insights, we aimed to characterize QFR-FFR disagreement with hemodynamic flow and resistance parameters as measured with Doppler-derived coronary flow. With use of FFR as reference standard, we hypothesized that (1) false negative QFR measurements can be explained by a high coronary flow reserve, and (2) that false positive QFR measurements can be explained with flow and resistance patterns suggestive of microvascular disease.

Methods

Study subjects

This sub study included all core-lab (Amsterdam University Medical Center, Amsterdam, the Netherlands) accepted pressure and flow data from patients enrolled in the DEFINE-FLOW study (NCT02328820). Study design and main results were previously described in-depth [12, 13]. Each local site received approval from its institutional review board. All subjects provided written informed consent prior to enrollment. In short, patients with symptoms suggestive of ischemic heart disease, invasive coronary angiography (ICA) defined diameter stenosis ≥ 50%, and reference diameter ≥ 2.5 mm were included for assessment of pressure and flow across all suitable lesions. The main exclusion criteria were prior coronary artery bypass graft surgery, left main disease requiring revascularization, vessel tortuosity precluding ComboWire advancement, severe left ventricular hypertrophy (septal wall thickness > 13 mm), contraindication to adenosine infusion, recent (within 3 weeks) ST-elevation myocardial infarction, culprit lesion in non-ST-elevation myocardial infarction, and life expectancy less than 24 months. We applied additional substudy specific exclusion criteria related to QFR including poor image quality, no available images, aorto-ostial lesions, and lesions on both side of bifurcations with a major shift (> 1 mm) in reference diameter.

Invasive hemodynamic measurements and treatment

The ComboWire XT (Philips Volcano, San Diego USA) was used for invasive physiologic assessment. Hyperemia was induced with 100 µg (or 60 µg if limiting arrhythmia) intracoronary adenosine for two consecutive measurements after advancing the wire distal to the lesion. PCI was performed in lesions with combined FFR ≤ 0.80 and CFR < 2.0 and deferred in discordant and concordant negative lesions. Based on the core-lab data, the following parameters were derived: (1) Resting Pd/Pa, iFR and FFR defined as the ratio of distal coronary pressure (Pd) and aortic coronary pressure (Pa) during resting, the wave-free period and hyperemic conditions, respectively; (2) Coronary flow reserve (CFR) defined as the ratio of peak hyperemic flow velocity to baseline peak flow velocity; (3) Hyperemic microvascular resistance (HMR) defined as the ratio of distal coronary pressure to maximal coronary flow velocity during hyperemia, and (4) Hyperemic stenosis resistance (HSR) defined as the ratio of the pressure gradient across a lesion and coronary flow velocity during hyperemia [14]. We used the average values from all approved measurements obtained with use of IC adenosine while the average of all approved IV measurements was used if IC was not available.

Quantitative flow ratio analysis

Contrast-flow based Quantitative Flow Ratio was computed in a core-lab setting (Aarhus University Hospital, Skejby, Denmark) by experienced analysts (J.W, H.M.R and M.S.H) following a dedicated SOP [15]. All observers were blinded to all study data except sex and indication of target vessel segment. The QFR value that corresponded to the pressure sensor position was used in analysis. In cases where the pressure-wire was not cined, the QFR value distal to all visuable disease was used.

Clinical follow-up

Subjects were followed every 6 months until the final 2-year visit. Events were adjudicated by an independent Clinical Event Committee. Target vessel failure (TVF) was defined as a composite of target vessel MI and revascularization (target vessel and target lesion).

Analysis strategy

Our main outcome was the numerical difference for CFR and HMR between the following lesion/vessel groups: FFR+QFR− vs. FFR+QFR+ lesions as well as FFR−QFR− vs. FFR−QFR+ lesions. Key secondary outcomes included the agreement of QFR with FFR, diagnostic performance of QFR and FFR with CFR as reference standard, agreement and diagnostic performance of QFR, FFR and CFR with HSR as reference standard, and the prognostic value of QFR for lesions that did not undergo revascularization during the index procedure.

Statistics

Data was stratified into 4 groups: FFR > 0.80 (−) & QFR > 0.80 (−); FFR ≤ 0.80 (+) & QFR > 0.80 (−); FFR ≤ 0.80 (+) & QFR ≤ 0.80 (+); and FFR > 0.80 (−) & QFR ≤ 0.80 (+). Continuous variables are presented as mean ± standard deviation or median with interquartile range (IQR) and categorical variables as number (%). The relationship between QFR and FFR was investigated using linear regression analysis and is illustrated with scatter and Bland–Altman plots. The relationship of QFR, FFR and CFR with HSR was illustrated with scatter-plots and the discriminatory ability was assessed with area under the receiver operating curve analysis. The lesions-specific anatomical and physiological parameters

were analyzed on a per-vessel and compared between the prespecified groups using the Kruskal–Wallis test. Sensitivity, specificity, predictive values and likelihood ratios were calculated for FFR and QFR with CFR as reference standard. Confidence interval for difference in sensitivity and specificity was calculated using Wald's method. The non-revascularized lesions were divided according to QFR level and the TVF rate was evaluated with Kaplan–Meier survival curves. QFR was further evaluated as a fixed continuous predictor for TVF rate adjusted for CFR and FFR using a mixed cox regression model accounting for multiple lesions per patient. Applied diagnostic cut-offs for FFR, QFR, CFR, HSR and HMR were ≤ 0.80, ≤ 0.80, < 2.0, > 0.80 and > 2.5. Analysis was conducted in R (R Foundation for Statistical Computing, Vienna, Austria).

Results

QFR was computed for 204 patients (234 lesions) out of 382 patients (456 lesions) with accepted core-lab data (Fig. 1). The majority of QFR-related exclusions were related to lack of matching images (e.g. acquisition of only 1 projection) (50%); poor image quality (18%), or no stored angiography (18%). Baseline characteristic are summarized in Table 1. Lesion characteristics are summarized stratified by QFR/FFR agreement in Table 2. Distribution of QFR and FFR is illustrated in Fig. 2.

Agreement between QFR and FFR

QFR correlated ($R = 0.64$) to FFR with agreement 0.003 ± 0.09 (Fig. 2). A total of 77% of all lesions showed diagnostic concordance with most (15%) discordance being FFR−QFR+ discordant lesions (central illustration). More QFR/FFR values were in the 0.77–0.83 range for discordant vs. concordant groups (Table 2). Contrast flow velocity as derived with the modified TIMI frame counting correlated weakly ($R = 0.29$) to baseline peak flow velocity and hyperemic peak flow velocity ($R = 0.21$).

Table 1 Baseline characteristics

	Total ($n = 204$)
Demographics	
Age (years)	67 ± 10
Male	142 (74)
Body mass index (kg/m^2)	26.3 ± 4.0
Risk factors	
Hypertension (202/204)	140 (69)
Dyslipidemia (203/204)	183 (90)
Family history (192/204)	78 (38)
Smoking (current or past) (193/204)	107 (55)
Diabetes (203/204)	59 (29)
Previous MI (202/204)	38 (19)
Angina severity	
No angina	69 (34)
CCS 1	48 (24)
CCS 2	46 (23)
CCS 3	22 (11)
CCS 4	19 (10)
Clinical presentation	
Asymptomatic or stable angina	162 (80)
Unstable angina	31 (15)
NSTEMI	11 (5)

CCS Canadian Cardiovascular Society grading of angina pectoris, *MI* myocardial infarction; and *NSTEMI* non-ST-elevation myocardial infarction

Comparison of hemodynamical and anatomical parameters

CFR was on average highest for FFR+QFR− lesions and only reduced (< 2.0) for concordant abnormal (FFR+QFR+) lesions, while HMR was highest for concordant normal (FFR−QFR−) lesion and lowest for FFR+QFR− lesion. CFR was higher and HMR lower for FFR+QFR− lesions when compared to FFR+QFR+ lesion (Fig. 3 and Table 2). CFR and HMR did not differ for FFR−QFR+ lesions when compared to FFR-QFR- lesions (Fig. 3 and Table 2). The remaining anatomical and physiological parameters were stratified by QFR/FFR correspondence and listed in Table 2. While baseline flow did not differ between the four groups,

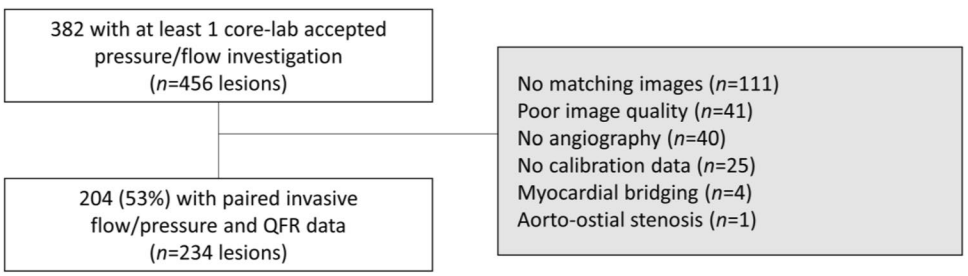


Fig. 1 Flowchart. QFR denotes quantitative flow ratio

Table 2 Lesion characteristics stratified by QFR and FFR correspondence

	Total ($n=234$)	FFR-QFR-($n=139$)	FFR−QFR+ ($n=34$)	FFR+QFR+ ($n=43$)	FFR+QFR−($n=18$)
Location					
RCA	34 (14)	22 (16)	4 (12)	5 (12)	3 (17)
LAD	156 (67)	84 (60)	25 (74)	33 (76)	14 (78)
LCx	44 (19)	33 (24)	5 (6)	5 (12)	1 (5)
Pressure					
Resting Pd/Pa	0.95 (IQR: 0.92–0.97)	0.96 (IQR: 0.94–0.99)	0.95 (IQR: 0.93–0.97)	0.87 (IQR: 0.86–0.91)	0.89 (IQR: 0.85–0.91)
iFR (196/234)	0.94 (IQR: 0.90–0.97)	0.96 (IQR: 0.93–0.99)	0.95 (IQR:0.92–0.97)	0.85 (IQR: 0.81–0.89)	0.89 (IQR: 0.84–0.91)
FFR	0.86 (IQR: 0.80–0.91)	0.89 (IQR: 0.86–0.94)	0.85 (IQR: 0.82–0.90)	0.72 (IQR: 0.66–0.76)	0.75 (IQR: 0.73–0.78)
QFR	0.86 (IQR: 0.77–0.93)	0.90 (IQR: 0.87–0.95)	0.76 (IQR: 0.72–0.78)	0.67 (IQR: 0.62–0.74)	0.88 (IQR: 0.84–0.91)
QFR/FFR 0.77–0.83	80 (34)	30 (22)	24 (71)	16 (37)	`10 (56)
Anatomy					
DS, %	48.3 (IQR: 40.2–55.5)	43.4 (IQR: 35.0–50.6)	55.2 (IQR: 51.7–61.3)	58.5 (IQR: 53.1–64.0)	45.5 (IQR: 41.5–52.5)
LL, mm	15.7 (IQR: 11.6–23.6)	14.5 (IQR: 9.7–20.1)	16.5 (IQR: 14.2–30.7)	24.4 (IQR: 15.2–29.6)	13.7 (IQR: 9.9–18.4)
AS, %	67.1 (IQR: 57.5–74.5)	61.3 (IQR: 49.5–69.2)	74.3 (IQR: 70.5–78.6)	74.8 (IQR: 70.1–81.9)	62.9 (IQR: 59.9–74.7)
MLD, mm	1.3 (IQR: 1.1–1.7)	1.5 (IQR: 1.2–1.8)	1.2 (IQR: 1.0–1.7)	1.0 (IQR: 0.9–1.3)	1.3 (IQR: 1.2–1.6)
RVD, mm	2.6 (IQR: 2.3–2.9)	2.6 (IQR: 2.3–3.0)	2.8 (IQR: 2.6–3.1)	2.5 (IQR: 2.2–2.8)	2.6 (IQR: 2.4–2.8)
Flow					
CFR	2.2 (IQR: 1.9–2.6)	2.2 (IQR: 1.9–2.6)	2.2 (IQR: 1.9–2.9)	1.9 (IQR: 1.5–2.4	2.3 (IQR: 2.1–2.7)
CFR < 2.00	77 (33)	37 (27)	12 (35)	25 (58)	3 (17)
bAPV, cm/s	15.3 (IQR: 12.4–19.3)	15.2 (IQR: 12.3–18.7)	13.7 (IQR: 11.8–21.0)	17.6 (IQR: 13.0–20.8)	15.6 (IQR: 13.5–18.4)
eCFV, cm/s	16.0 (12.0–21.0)	16.0 (IQR: 12.0–22.0)	15.0 (IQR: 13.0–20.0)	17.0 (IQR: 13.5–21.0)	14.0 (IQR: 13.0–16.0)
hAPV, cm/s	33.2 (25.0–39.8)	33.6 (IQR: 25.3–39.4)	35.4 (IQR: 24.2–40.0)	28.1 (IQR: 22.6–36.4)	33.7 (IQR: 30.1–429)
Resistance					
HMR, mmHg/cm/s	2.39 (IQR: 1.86–3.01)	2.57 (IQR: 2.01–3.22)	2.34 (IQR: 1.85–2.81)	2.26 (IQR: 1.79–2.87)	1.72 (IQR: 1.48–2.31)
HSR, mmHg/cm/s	0.37 (IQR: 0.24–0.60)	0.27 (IQR: 0.18–0.41)	0.38 (IQR: 0.24–0.48)	0.84 (IQR: 0.70–1.17)	0.64 (IQR: 0.41–0.73)

Remaining abbreviation as in Figs. 1 and 2

RCA right coronary artery, *LAD* left anterior descending artery, *LCx* left circumflex artery, *Pd* distal coronary pressure, *Pa* proximal coronary pressure, *DS* diameter stenosis, *LL* lesion length, *AS* area stenosis, *MLD* minimum lumen diameter, *RVD* reference vessel diameter, *bAPV* baseline average peak flow velocity, *eCFV* estimated contrast flow velocity; and *hAPV* hyperemic peak flow velocity; and *HSR* hyperemic stenosis resistance

peak hyperemic flow velocity was higher and hyperemic stenosis resistance lower for FFR+QFR− lesions compared to FFR+QFR+ lesions (Table 2). iFR tended to be higher for FFR+QFR− lesions than for FFR+QFR+ lesions. FFR+QFR− were anatomically milder (lower %DS, larger minimum lumen diameter and shorter lesion length) as compared to FFR+QFR+ lesions, while FFR−QFR+ were more severe (larger %DS, lower minimum lumen diameter, and longer lesion length) than FFR−QFR− lesions (Table 2).

Diagnostic performance of QFR and FFR

Using CFR (< 2.0) as reference standard, FFR and QFR were comparable in diagnostic performance estimates

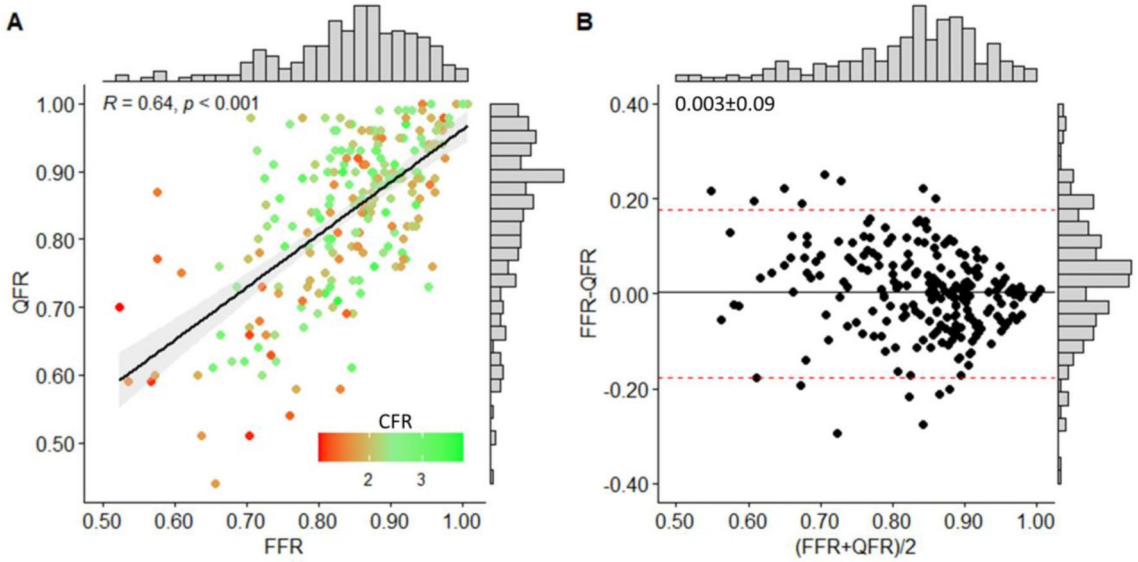


Fig. 2 Bias and imprecision of QFR. Correlation (**A**) and agreement (**B**) of QFR with FFR as reference standard. Distribution of the variables is illustrated with marginal histograms. Scatter plot is color-coded according to the underlying coronary flow reserve value. Black and red lines in panel **B** indicate difference and 95% limits of agreement. QFR denotes quantitative flow ratio and FFR denotes fractional flow reserve

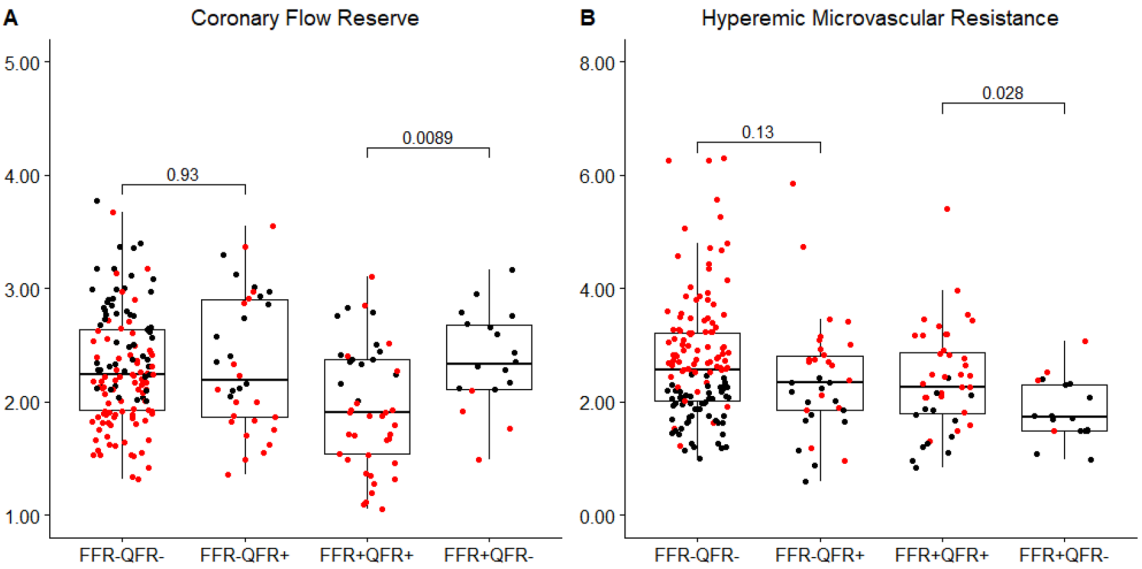


Fig. 3 Coronary flow reserve and hyperemic microvascular resistance stratified according to QFR/FFR agreement. Red colored points indicate CFR < 2.0 or HMR > 2.5. CFR denotes Coronary Flow Reserve and HMR denotes hyperemic microvascular resistance. Remaining abbreviations as in Fig. 1

although with a lower false negative rate for QFR as depicted by a difference in sensitivity of 11.7% (95% CI 2.2–21.2) (Table 3). The agreement and diagnostic performance of FFR using HSR (> 0.80) as reference standard was higher compared with QFR and CFR mediated by fewer false positive FFR values (lower left quadrants in Fig. 4).

Clinical outcomes

In lesions (n = 195) not revascularized, a total of 9 TVF occurred as 8 TLR and 1 TVR during 2 years of follow-up. Vessels with QFR ≤ 0.80 (23%) showed a higher TVF (11.1% vs. 2.7%) rate as compared to vessel with QFR > 0.80 (Fig. 5). The difference [8.4% (95% CI 0.4–19.1)] was

Table 3 Diagnostic performance of FFR and QFR with CFR as reference

	FFR	*QFR*
Sensitivity	36.4 (25.6–59.2)	48.1 (36.9–59.2)
Specificity	79.0 (72.6–85.4)	74.5 (67.7–81.3)
PPV	45.9 (33.4–58.4)	48.1 (36.9–59.2)
NPV	71.7 (65.0–78.4)	74.5 (67.7–81.3)
LR (+)	1.73 (1.13–2.64)	1.89 (1.32–2.69)
LR (−)	0.81 (0.67–0.97)	0.70 (0.55–0.88)

Remaining abbreviations as in Fig. 1

PPV denotes positive predictive value, *NPV* negative predictive value, *LR* (+) positive likelihood ratio; and *LR* (−) negative likelihood ratio

statistically significant. An increase of 0.10 for QFR indicated an association with a reduction in TVF [HR 0.54 (95% CI 0.28–1.03)]. Group distribution of TVF was 4(3%), 0(0%), 2(15%), 3(9%) in the FFR−QFR−, FFR+QFR−, FFR+QFR+ and FFR−QFR+ groups.

Discussion

The main findings were that (1) FFR+QFR− lesions had a flow, resistance, and anatomic profile different from FFR+QFR+ lesions but were comparable to FFR−QFR− lesions; (2) FFR−QFR+ lesions did not differ from FFR-QFR- lesions in hemodynamic parameters but were anatomically more severe; (3) QFR ≤ 0.80 was frequently observed in non-revascularized lesions and was related to TVF during follow-up.

Since the initial presentation of complex and time-consuming computational fluid dynamic simulations used to derive FFR from angiography, current fluid-equation based solutions are faster owing to computations based on simpler hemodynamic laws [16–18]. This has led to concerns if the simpler computation could be inaccurate in specific anatomical and/or physiological presentations such as serial lesions, diffuse disease, co-existing aortic valve disease and

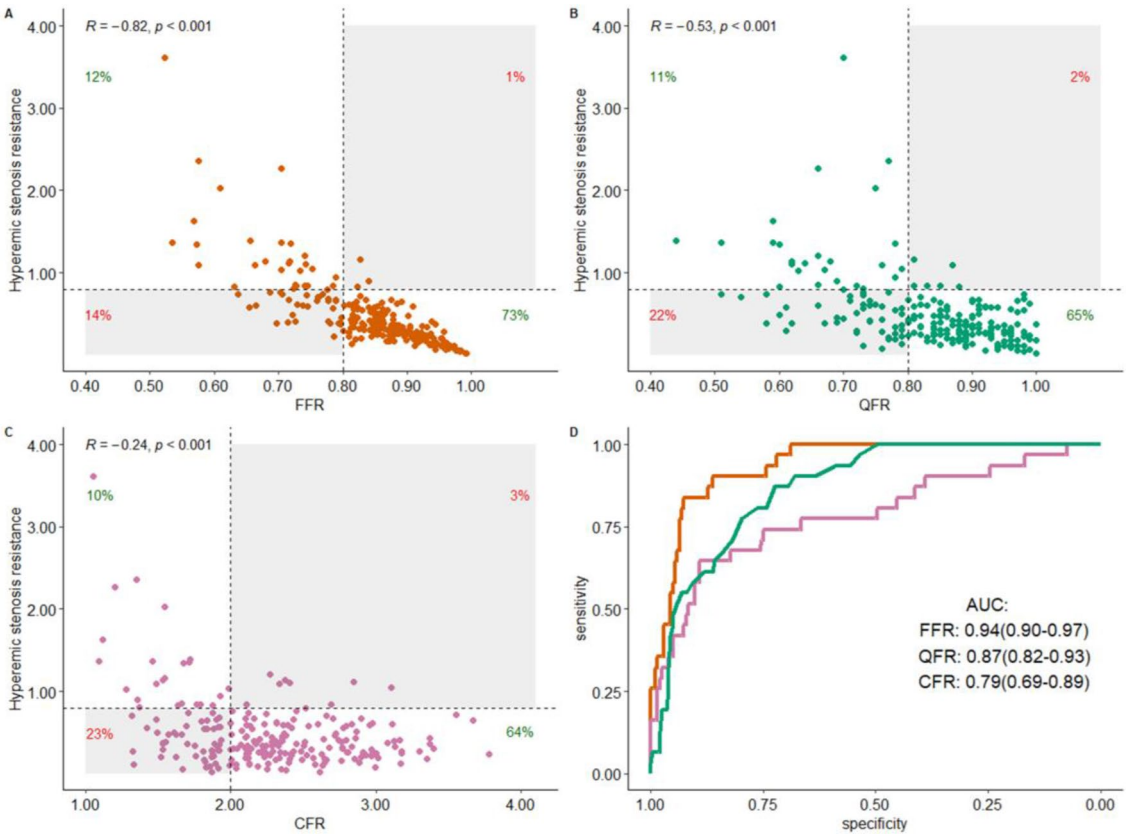


Fig. 4 Agreement with hyperemic stenosis resistance. The correlation and diagnostic agreement of FFR (**A**), QFR (**B**) and CFR (**C**) with hyperemic stenosis resistance as reference. FFR had a better discriminatory ability to identify stenoses with high hyperemic stenosis resistance (**D**). Abbreviations as in Figs. 1 and 2

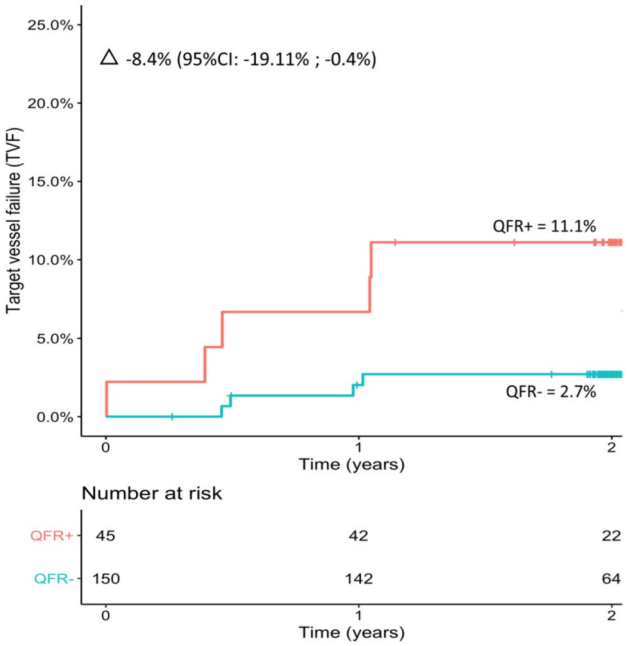


Fig. 5 Clinical outcomes in population not revascularized during index procedure. Target vessel failure (TVF) according to groups stratified by QFR (≤/>0.80). TVF was defined as a composite of MI and revascularization on a per-lesion level. Abbreviations as in Fig. 2

microvascular disease. Our study now provides further mechanistic insights into anatomical and physiological patterns explaining FFR/QFR discordance.

The presented findings illustrate the challenges related to simulation of complex biological physiological mechanisms using fluid algorithms. The latter is backed by the observation that all invasive measurement (e.g. FFR, iFR and resting Pd/Pa) were on average in agreement for FFR vs. QFR discordant lesions (Table 2). FFR+QFR− lesions were anatomically mild, had low iFR and resting Pd/Pa values, a high hyperemic peak flow velocity and a healthy microcirculation (low HMR) translating to normal/high CFR values. The hemodynamic and anatomical profile of FFR+QFR− lesions is in line with previously acquired data with thermodilution and also with a previous study describing FFR+iFR− lesions with Doppler flow [9, 19]. Furthermore, we did not observe any TVF for this group during 2 years of follow-up although the sample size was small. However, deferring revascularization of FFR+CFR− lesions is not non-inferior to the clinical outcome of FFR−CFR− lesions, although the event rate, determined by elective PCI is low in both groups [13]. It thus remains to be seen if QFR's false negative rate translates into impaired outcome.

The FFR−QFR+ lesions did not have a physiological profile confirmative of microvascular disease as previously suggested [9, 10]. In fact, HMR was highest for FFR-QFR- lesions potentially because the TIMI frame count needed in QFR-computation may also be affected by downstream resistance disorders [20]. Furthermore, resting Pd/Pa and iFR values were high (Table 2). Hence, previous findings describing that anatomical severe lesions tend to cause a large FFR > QFR difference seems to be the most plausible explanation for FFR−QFR+ mismatches. This would fit with our finding that lesions with FFR−QFR+ were anatomically more severe than lesions with FFR−QFR− [7, 9]. Difficulties related to deriving a correct reference function in diffuse disease and/or contouring of tight lesions could be major contributors to the difference. Additionally, variability of FFR and QFR added to the discordance rates because values close to 0.80 cut-point were more prevalent in the discordance groups (Table 2).

Quantitative flow ratio incorporates a flow component in form of the modified TIMI frame-count. However, similar to CFR, it is affected by variations in baseline flow that may not be caused by epicardial disease. On the contrary, HSR is considered a specific measure for epicardial lesion severity because HSR adjusts the trans-lesional pressure-gradient for the underlying hyperemic flow conditions [14]. In this regard, our results indicate that FFR and QFR are better estimators of epicardial lesion severity than CFR with FFR outperforming QFR using HSR as reference (Fig. 4).

In the DEFINE-FLOW study, lesions were only revascularized if both CFR and FFR were positive (FFR ≤ 0.80 and CFR < 2.0). We found that QFR was able to identify untreated vessels prone to cause TVF during follow-up and that QFR tended to have a continuous association with TVF similar to what was previously found for FFR but not CFR. However, the limited number of patients studied and the low event rate preclude to draw definitive conclusions. These findings justify and lay the foundation for ongoing outcome clinical outcome trials with head-to-head comparison of QFR and FFR for the guidance of PCI [21].

Limitations

Our analysis was hampered by the low feasibility of QFR due to the lack of prespecified acquisition protocol. Most exclusions were related to factors that made it impossible to attempt QFR (no matching images, no stored angiography and lack of calibration data). The true feasibility rate (success rate per attempt) was thus closer to previous studies where QFR was computed in a core-lab setting [10]. Additionally, pressure-sensor position was not cined for a number (~10%) of cases which may have impacted the QFR vs. FFR discordance rate. Further, physiological indices are not fully appreciated in a binary fashion as done for the primary analyses in the current rapport [22]. Hence, the QFR outcome analysis was also performed using QFR as a continuous index. The outcome analysis was limited by few events and is thus only hypothesis generating in nature. The

analysis would statistically be more powerful if including the entire sample and by studying global MACE (primary endpoint of DEFINE-FLOW). However, we would not be able to adjust for treatment (e.g., PCI) that could possibly impact the analysis. Further, physiology in one vessel may not be responsible for events in a second vessel and TVF was therefore deemed more suitable for this analysis. Finally, this paper provides a mechanistic understanding of FFR and QFR disagreement because only a randomized clinical outcome study can truly inform on the importance of QFR and FFR disagreement.

Conclusion

Disagreement between FFR and QFR can partly be explained with physiological and anatomical factors.

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Declarations

Conflict of interest Dr. Mejia-Renteria has received consultancy fees from Medis Medical Imaging and speaker fees from Philips and Abbott out of the submitted work. Dr. Evald Christiansen received research grants from Medis and Philips/Volcano to his institution outside of the submitted work. The remaining authors have no disclosures to report.

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