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Comparison of resting distal to aortic coronary pressure with angiography-based quantitative flow ratio

Barbara E. Stähli [a,b,1], Aslihan Erbay [a,b,1], Julia Steiner [a,b,1], Jens Klotsche [c,d,1], Hans-Christian Mochmann [a,b,1], Carsten Skurk [a,b,1], Alexander Lauten [a,b,1], Ulf Landmesser [a,b,e,1], David M. Leistner [a,b,e,*,1]

[a] Department of Cardiology, Charité Berlin – University Medicine, Campus Benjamin Franklin, Berlin, Germany
[b] DZHK (German Centre for Cardiovascular Research), partner site Berlin, Berlin, Germany
[c] German Rheumatism Research Center Berlin, Berlin, Germany
[d] Institute for Epidemiology and Health Care Economics, Charité Berlin – University Medicine, Campus Mitte, Berlin, Germany
[e] Berlin Institute of Health (BIH), Berlin, Germany

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ABSTRACT

Background: Quantitative flow ratio (QFR) is a novel, adenosine-free method for functional coronary lesion interrogation, which is based on 3-dimensional quantitative coronary angiography and computational algorithms. Data on QFR in all-comer patients with intermediate coronary lesions are scarce, and the diagnostic performance in comparison to resting distal to aortic coronary pressure (Pd/Pa) ratio unknown.
Methods: A total of 436 patients with 516 vessels undergoing FFR measurements were included in the analysis. Diagnostic performance of QFR, distal to aortic coronary pressure (Pd/Pa) ratio, and anatomic indices versus FFR was assessed.
Results: FFR ≤0.80 was measured in 19.4% of interrogated vessels. QFR significantly correlated with FFR ($r = 0.82$, $p < 0.001$) with good agreement between QFR and FFR (mean difference 0.011, 95% CI 0.008–0.015). The AUC for an FFR ≤0.80 was 0.86 (95% CI 0.83–0.89, $p < 0.001$) for QFR, 0.76 (0.72–0.80, $p < 0.001$) for resting Pd/Pa ratio, and 0.63 (0.59–0.67, $p < 0.001$) for diameter stenosis. The diagnostic accuracy for identifying an FFR ≤0.80 was 93.4% for QFR, 84.3% for resting Pd/Pa ratio, and 80.4% for diameter stenosis.
Conclusions: QFR provides a novel diagnostic tool for functional coronary lesion assessment with superior diagnostic accuracy as compared with resting Pd/Pa ratio and anatomic indices. Future studies are needed to determine the non-inferiority of QFR analysis to FFR assessment with respect to clinical outcomes.

1. Introduction

Assessment of functional coronary lesion significance by conventional angiography is limited and associated with substantial interobserver variability [1–3]. Pressure-derived fractional flow reserve (FFR) is considered the gold standard for functional coronary lesion interrogation [4,5], with FFR-guided percutaneous coronary intervention (PCI) being related with favourable outcomes as compared with angiography alone [6,7]. Fractional flow reserve, however, is not systematically used prior to PCI due to technical challenges, prolonged procedure time, and incurred costs [8]. Further, FFR is based on the induction of hyperemia and adverse effects related to adenosine may limit its use. Novel adenosine-free coronary indices have therefore been developed to overcome these limitations [9–11].

Quantitative flow ratio (QFR) is a novel, image-based measure developed for the functional assessment of coronary lesion severity, which is based on three-dimensional quantitative coronary angiography (3D-QCA) and advanced computational algorithms [12], thereby avoiding the need for invasive pressure measurements and induction of hyperemia [10,13,14]. Most recently, the FAVOR (Functional Assessment by Various Flow Reconstructions) studies have demonstrated the accuracy of QFR in the hemodynamic assessment of coronary lesion severity [10,14]. Data on QFR in all-comer patients with intermediate coronary lesions are scarce, and the diagnostic performance of QFR in comparison to other non-hyperemic indices such as resting distal to aortic coronary pressure (Pd/Pa) ratio is uncertain.

The aim of this study was therefore to assess the diagnostic performance of QFR versus FFR and non-hyperemic indices in a large, real-world patient cohort with intermediate coronary lesions.

* Corresponding author at: Department of Cardiology, Charité Berlin – University Medicine, Campus Benjamin Franklin, Berlin, Germany.
E-mail address: david-manuel.leistner@charite.de (D.M. Leistner).
[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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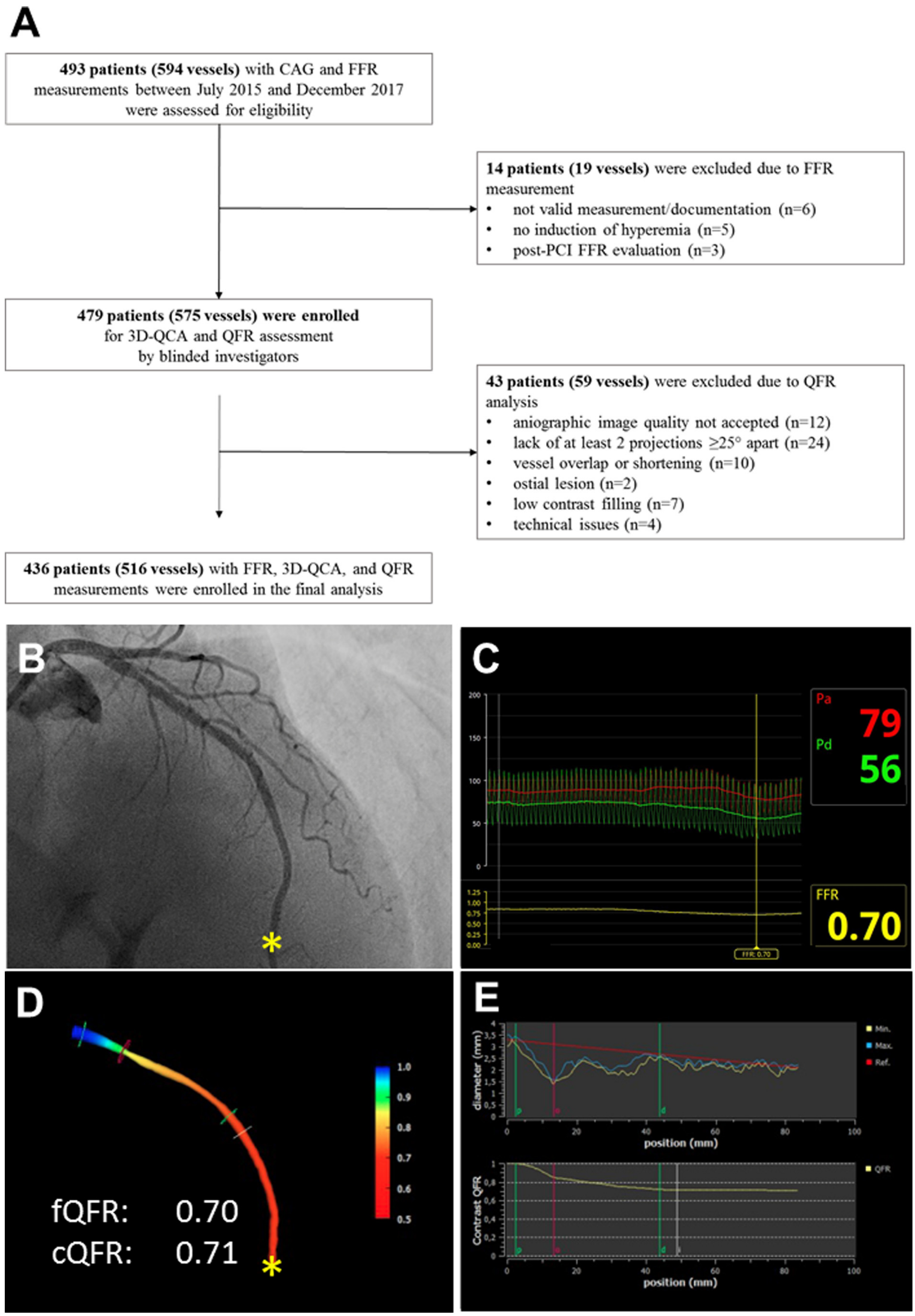
A
493 patients (594 vessels) with CAG and FFR measurements between July 2015 and December 2017 were assessed for eligibility
14 patients (19 vessels) were excluded due to FFR measurement
• not valid measurement/documentation (n=6)
• no induction of hyperemia (n=5)
• post-PCI FFR evaluation (n=3)
479 patients (575 vessels) were enrolled for 3D-QCA and QFR assessment by blinded investigators
43 patients (59 vessels) were excluded due to QFR analysis
• aniographic image quality not accepted (n=12)
• lack of at least 2 projections ≥25° apart (n=24)
• vessel overlap or shortening (n=10)
• ostial lesion (n=2)
• low contrast filling (n=7)
• technical issues (n=4)
436 patients (516 vessels) with FFR, 3D-QCA, and QFR measurements were enrolled in the final analysis
B
C
Pa
79
Pd
56
FFR
0.70
D
fQFR: 0.70
cQFR: 0.71
E
diameter (mm)
position (mm)
Min.
Max.
Ref.
Contrast QFR
position (mm)
QFR

2. Methods

2.1. Study population

A total of 436 consecutive patients with 516 intermediate coronary lesions (defined as 40% to 70% diameter stenosis by visual estimation), who underwent coronary angiography and FFR measurements at our institution between July 2015 and December 2017, were included in the analysis (Fig. 1A). No non-study FFR interrogations were performed in these patients. Fractional flow reserve measurements were performed according to current guidelines and recommendations [4,5]. Pressure tracings for FFR and resting Pd/Pa ratio measurements were independently adjudicated post hoc, and measurements of QFR performed at the institution's core laboratories. The study was conducted in accordance with the principles of the Declaration of Helsinki and in accordance with local law and regulations. Ethical approval of the institutional review board was obtained.

In this study, patients with native de novo coronary lesions were included. De novo lesions were defined as coronary lesions that have not previously been treated with either angioplasty or stenting. Exclusion criteria comprised coronary artery bypass grafting to interrogated vessels, suboptimal documentation of FFR-measurements, suboptimal angiographic image quality, lack of at least 2 projections ≥25° apart, vessel overlap or shortening, ostial lesions, suboptimal contrast filling, and other technical issues impeding high-quality QFR analysis.

2.2. Three-dimensional quantitative coronary angiography

Three-dimensional quantitative coronary angiography was performed offline using validated software (QAngio XA/3D, Medis, Leiden, the Netherlands) [10,13,15]. Mean diameter of the proximal and distal reference vessels, minimum lumen diameter (MLD), percent diameter stenosis, percent area stenosis, and lesion length were measured by 3D-QCA.

2.3. Fractional flow reserve

Standardized FFR and resting Pd/Pa measurements were performed under therapeutic anticoagulation (5000 units of unfractionated heparin) and maximal vasodilation (200 μg nitroglycerin) using a 6F coronary guiding catheter and a dedicated 0.014-inch coronary pressure guidewire (Certus™ and Aeris™, St. Jude Medical, St. Paul, MN, USA, Fig. 1B and C) [16]. Calibration of pressure systems was performed prior to pressure guidewire insertion. After intracoronary administration of nitroglycerin, pressures were equalized with the pressure sensor placed 1 to 2 mm distally to the tip of the coronary guiding catheter. The pressure guidewire was then advanced into the target coronary artery with the pressure sensor placed at least 2 to 3 cm distally to the coronary artery stenosis. Resting Pd/Pa was calculated as the mean pressure distal to the stenosis divided by the mean aortic pressure over the whole cardiac cycle. Then, stable maximal hyperemia was induced by intravenous infusion of adenosine (140 μg/kg of body weight/minute for ~2 min) and arterial pressures were recorded simultaneously from the pressure guidewire transducer and the guiding catheter tip to calculate FFR values. Then, the pressure sensor was pulled back to the catheter tip to identify any pressure drift. For the purpose of this study, all pressure tracings were reviewed for high signal quality, and FFR and resting Pd/Pa ratio analyzed offline by experienced investigators blinded to QFR. Fractional flow reserve measurements were used as standard reference.

2.4. Quantitative flow ratio

Quantitative flow ratio was calculated as previously described using validated software (QAngio XA/3D, Medis, Leiden, the Netherlands, Fig. 1D and E) [10,13,14]. Analyses were performed by certified investigators blinded to FFR and resting Pd/Pa ratio values and according to QCA standard operation procedures. Fixed-flow and contrast-flow vessel QFR are calculated using computational algorithms and 3D vessel reconstruction derived from 2 angiographic projections at least 25° apart [10,12,15]. The vessel segment used for vessel QFR analyses starts proximal close to the coronary ostium, but distal to the guiding catheter, and ends at the position of the pressure sensor located at the proximal end of the radiopaque wire tip. Fixed-flow vessel QFR is based on the assumption of a fixed empiric hyperemic flow velocity of 0.35 m/s, and contrast-flow vessel QFR on a modelled hyperemic flow velocity derived from frame counting on the diagnostic angiographic projection with the best image quality and the most well-defined contrast flow without induction of hyperemia, respectively [10].

2.5. Statistical analysis

Continuous variables are presented as mean and standard deviation (SD) or median and interquartile range, and categorical variables as frequencies and percentages. Shapiro-Wilk test was used to test whether a parameter followed a normal distribution. Data were analyzed at the patient level for baseline clinical and procedural characteristics and at the vessel level for functional coronary indices. A linear regression model was used to compare vessel QFR, resting Pd/Pa ratio, and FFR. Correlations between two variables were specified by the Spearman's rank correlation coefficient. Bland-Altman plots tested the agreements between vessel QFR, resting Pd/Pa ratio, and FFR. The diagnostic performance of vessel QFR, resting Pd/Pa ratio, and anatomic indices for predicting hemodynamically significant intermediate coronary artery lesions as defined by an FFR ≤0.80 was assessed by sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, and diagnostic accuracy. Receiver-operating characteristic (ROC) curves were constructed to assess the diagnostic accuracy of vessel QFR, resting Pd/Pa ratio, and anatomic indices for identifying an FFR ≤0.80 as a reference standard using area under the curves (AUCs) with 95% confidence intervals [6]. Differences between AUCs were tested with the DeLong method. Cut-off values of ≤0.80 for vessel QFR [10,14], ≤0.91 for resting Pd/Pa ratio [9], ≤1.20 mm for MLD [13], >50% for diameter stenosis [10,14], and ≥58% for area stenosis were based on prior studies [13]. A two-sided p-value of <0.05 was considered statistically significant. Receiver-operating characteristic curve analyses were performed using MedCalc version 18 (MedCalc Software, Ostend, Belgium), all other analyses using IBM-SPSS version 24 (IBM Corp., Chicago, IL, USA), respectively.

3. Results

3.1. Baseline characteristics

Patient baseline and procedural characteristics are summarized in Table 1. Median age of the patients (32.1% women) was 71.5 [63.0–77.0] years. The burden of cardiovascular comorbidities was high with 87.8% of patients having hypertension, 79.1% dyslipidemia, and 22.5% diabetes, respectively. Minimum lumen diameter of the interrogated vessels was 1.7 [1.4–1.9] mm and percent diameter stenosis 41 [36–46] %, with hemodynamic significance defined as an FFR of ≤0.80 observed in 100 (19.4%) vessels (Table 1).

3.2. Correlation of QFR with FFR

Median contrast-flow vessel QFR was 0.89 [0.84–0.93]. Strong correlations ($r = 0.82$, $p < 0.001$ for contrast-flow vessel QFR; and $r = 0.79$, $p < 0.001$ for fixed-flow vessel QFR) and good agreement in Bland-Altman analysis (mean difference 0.011, 95% CI 0.008–0.015, for contrast-flow vessel QFR; and mean difference 0.005, 95% CI 0.002–0.009, for fixed-flow vessel QFR) were observed for vessel QFR and FFR (Fig. 2A–C).

Median resting Pd/Pa ratio was 0.95 [0.92–0.98]. Resting Pd/Pa ratio significantly correlated with FFR ($r = 0.76$, $p < 0.001$) and had a good agreement in Bland-Altman analysis (Fig. 2A–C). Anatomical indices had weak correlations with FFR ($r = 0.35$, $p < 0.001$ for MLD; $r = -0.42$, $p < 0.001$ for percent diameter stenosis, and $r = -0.37$, $p < 0.001$ for percent area stenosis).

3.3. Diagnostic performance of QFR, resting Pd/Pa ratio, and anatomic indices

In ROC analysis, vessel QFR had a better accuracy in identifying an FFR ≤0.80 as compared with resting Pd/Pa ratio and anatomic indices (Fig. 2D). The AUCs for continuous contrast-flow vessel QFR, fixed-flow vessel QFR, and resting Pd/Pa ratio values were 0.98 (0.97–0.99, $p < 0.001$), 0.97 (0.96–0.98, $p < 0.001$), and 0.90 (0.96–0.93, $p < 0.001$), respectively. Corresponding values for MLD, percent diameter stenosis, and percent area stenosis were 0.72 (0.66–0.77, $p < 0.001$), 0.76 (0.71–0.81, $p < 0.001$), and 0.74 (0.69–0.79, $p < 0.001$).

Using a cut-off value of ≤0.80 for vessel QFR, the AUCs for contrast-flow vessel QFR and fixed-flow vessel QFR were 0.86 (95% CI 0.83–0.89, $p < 0.001$) and 0.84 (95% CI 0.81–0.87, $p < 0.001$), respectively. The AUC was 0.76 (0.72–0.80, $p < 0.001$) for resting Pd/Pa ratio ≤ 0.91, 0.58 (0.54–0.63, $p = 0.009$) for MLD ≤1.20 mm, 0.63 (0.59–0.67, p <

Fig. 1. Study flow chart and representative quantitative flow ratio (QFR) measurement of an intermediate coronary lesion in the left anterior descending coronary artery. A. Study flow chart. B. Right anterior oblique projection of the left coronary artery. C. Pressure tracings and fractional flow reserve (FFR) measured with the pressure sensor placed in the distal left coronary artery (yellow asterisk). D. QFR measurement. E. QFR pullback and lumen diameter with p representing proximal lesion marker, d distal lesion marker, and c lesion core. CAG = coronary angiography, FFR = fractional flow reserve, PCI = percutaneous coronary intervention, 3D-QCA = three-dimensional quantitative coronary angiography, and QFR = quantitative flow ratio.

0.001) for >50% diameter stenosis, and 0.66 (0.62–0.70, $p < 0.001$) for ≥58% area stenosis, respectively. The AUC for contrast-flow vessel QFR was significantly higher than the one for resting Pd/Pa ratio with a difference between areas of 0.11 (95% CI 0.04–0.17, $p = 0.001$). Similar results were observed for fixed-flow vessel QFR and resting Pd/Pa ratio (difference between areas 0.08, 95% CI 0.02–0.15, $p = 0.009$). No difference between areas was observed for contrast-flow and fixed-flow vessel QFR (0.02, 95% CI −0.02–0.06, $p = 0.32$). The AUCs for all resting indices were significantly higher than those for anatomic indices ($p < 0.05$).

Table 1
Baseline characteristics.

Patient characteristics (N = 436)	
Age, years	71.5 [63.0–77.0]
Female sex	140 (32.1)
BMI, kg/m^2	26.0 [23.9–29.2]
BSA, m^2	1.93 [1.79–2.05]
Cardiovascular risk factors	
Diabetes mellitus	98 (22.5)
Hypertension	383 (87.8)
Dyslipidemia	345 (79.1)
Smoking history	148 (34)
Family history of CAD	62 (14.2)
Medical history	
Known CAD	275 (63.1)
Prior CABG	11 (2.5)
Prior PCI	239 (54.8)
Prior myocardial infarction	143 (32.8)
Prior stroke/TIA	40 (9.2)
Peripheral vascular disease	25 (5.7)
Chronic obstructive pulmonary disease	37 (8.5)
Atrial fibrillation	108 (24.8)
Clinical presentation	
Stable CAD	313 (71.8)
Unstable angina	105 (24.1)
NSTEMI	18 (4.1)
Coronary artery disease extent	
Single vessel disease	146 (33.5)
Two vessel disease	167 (38.3)
Three vessel disease	123 (28.2)
LVEF (echocardiography), %	63 [55–70] (n = 327)
Patients with FFR measurement in >1 vessel	80 (15.05)
Radial access	349 (80.0)
Flouroscopy time, min	8.5 [6.1–12.7] (n = 433)
Amount of contrast media, ml	120 [85–160] (n = 432)
Dose-area product, cGy ∗ cm^2	2053 [1387–3106] (n = 432)
Vessel characteristics (N = 516)	
Target vessel	
Left anterior descending coronary artery	287 (55.6)
Diagonal branch	15 (2.9)
Left circumflex coronary artery	67 (13.0)
Obtuse marginal branch	23 (4.5)
Intermediate coronary artery	5 (1.0)
Right coronary artery	119 (23.1)
Bifurcation lesions	68 (13.2)
Resting distal-to-aortic pressure ratio	0.95 [0.92–0.98]
Fractional flow reserve	0.88 [0.82–0.92]
Fractional flow reserve ≤0.80	100 (19.4%)
Fixed-flow vessel quantitative flow ratio	0.89 [0.82–0.93]
Contrast-vessel quantitative flow ratio	0.89 [0.84–0.93]
Mean reference vessel diameter (3D-QCA), mm	2.8 [2.5–3.2]
Minimum lumen diameter (3D-QCA), mm	1.7 [1.4–1.9]
Percent diameter stenosis (3D-QCA), %	41 [36–46]
Diameter stenosis <40%	210 (40.7)
Diameter stenosis 40–70%	305 (59.1)
Diameter stenosis >70%	1 (0.2)
Percent area stenosis (3D-QCA), %	57 [49–64]
Lesion length (3D-QCA), mm	17.2 [12.0–24.9]

Values are given as median and interquartile range, or numbers and percentages. BMI = body mass index, BSA = body surface area, CAD = coronary artery disease, CABG = coronary artery bypass grafting, 3D-QCA = three-dimensional quantitative coronary angiography, FFR = fractional flow reserve, NSTEMI = non ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, TIA = transient ischemic attack, LVEF = left ventricular ejection fraction.

Diagnostic accuracy, sensitivity, and specificity of vessel QFR, resting Pd/Pa ratio, and anatomic indices in the prediction of an FFR ≤0.80 are summarized in Table 2. The diagnostic accuracy for identifying an FFR of ≤0.80 was 93.4% for contrast-flow vessel QFR ≤0.80 and 84.3% for resting Pd/Pa ratio ≤0.91. The positive and negative predictive values of contrast-flow vessel QFR were 89.3% and 94.2%, and corresponding values of resting Pd/Pa ratio 59.0% and 90.8%, respectively.

When incorporating only patients with FFR values around the threshold (0.75 to 0.85), the diagnostic performance was lower (n = 173). The diagnostic accuracy for identifying an FFR of ≤0.80 was 80.9% for contrast-flow vessel QFR ≤0.80 and 64.2% for resting Pd/Pa ratio ≤0.91. The positive and negative predictive values of contrast-flow vessel QFR were 84.6% and 79.3%, and corresponding values of resting Pd/Pa ratio 55.6% and 69.1%, respectively. Using a cut-off value of ≤0.80 for vessel QFR, the AUCs for contrast-flow vessel QFR and resting Pd/Pa were 0.78 (95% CI 0.70–0.86, $p \leq 0.001$) and 0.62 (95% CI 0.53–0.71, $p = 0.08$), respectively.

4. Discussion

This study demonstrates the high diagnostic performance of QFR versus FFR in a large, real-world patient cohort with intermediate coronary lesions. Importantly, hemodynamic lesion assessment by QFR outperformed resting Pd/Pa ratio and anatomic indices. These results further add to the evidence to support the use of OFR as a promising alternative to pharmacologic hyperemia for functional coronary lesion evaluation.

4.1. Assessment of intermediate coronary lesions

As visual estimation of coronary lesion severity based on conventional angiography alone is limited [1,2], pressure-derived FFR has been developed for the evaluation of functional lesion significance and is recommended by guidelines when documentation of ischemia by non-invasive testing is unavailable [4,5]. Contraindications such as asthma or chronic obstructive pulmonary disease, hypotension, technical obstacles, and incremental costs, however, may restrict its use and have fuelled the search for novel adenosine-free indices such as resting Pd/Pa ratio and instantaneous wave-free ratio (iFR) [8–10,17]. A growing number of studies have recently reported on the equivalent agreement of resting Pd/Pa ratio and iFR with FFR [18–20], suggesting that resting measures could be used as less invasive alternatives to pharmacologic hyperemia.

4.2. Diagnostic performance of QFR

Quantitative flow ratio is an emerging, image-based tool for advanced functional lesion interrogation, which is solely based on 3D-QCA and dedicated computational algorithms, thereby avoiding the need for invasive pressure measurements [10,13,14,21]. Its adenosine-free ability for hemodynamic lesion assessment avoids procedure-related symptoms related to hyperemia and may be particularly useful in patients with any contraindications to FFR. Coronary angiography-derived FFR (FFR_{angio}) bears similar advantages, as this modality is also solely based on the coronary angiogram and a dedicated computational algorithm and provides a three-dimensional model of the coronary artery tree [22,23]. In comparison to wire-based FFR, FFR_{angio} and QFR integrate both anatomical and functional information and may therefore be particularly useful in tandem lesions or diffuse disease. Which one of the two methods will turn out to be more accurate and less operator dependent remains to be determined in future studies. A diagnostic strategy of first-line coronary computed tomography (CT) angiography in symptomatic patients with suspected coronary artery disease, and CT-derived FFR testing in those with intermediate coronary lesions may be effective in differentiating patients who do not require further diagnostic testing or intervention from higher-risk patients in

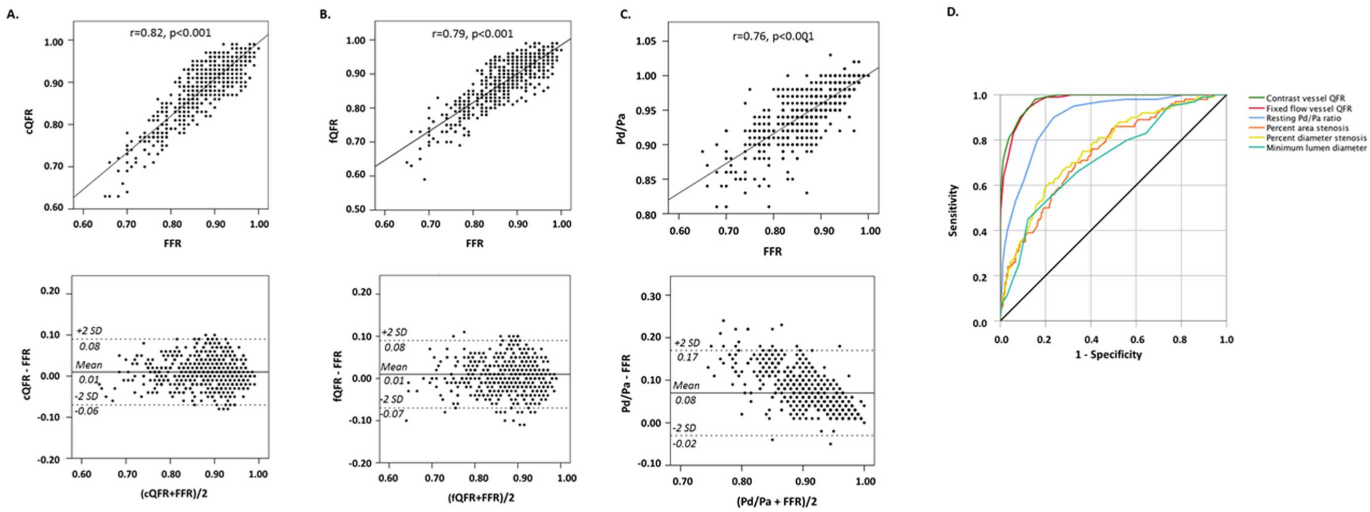

Fig. 2. Correlation and agreement between quantitative flow ratio (QFR), resting distal to aortic coronary pressure (Pd/Pa) ratio, and fractional flow reserve (FFR) measurements. A. Correlation and Bland Altmann plot between contrast-flow vessel QFR and FFR. B. Correlation and Bland Altmann plot between fixed-flow vessel QFR and FFR. C. Correlation and Bland Altmann plot between resting Pd/Pa ratio and FFR. D. Receiver-operating characteristic (ROC) curves for predicting an FFR ≤0.80.

whom further testing with invasive coronary angiography and possible intervention is needed [24,25]. In this study, representing the largest study on the performance of QFR to date, a rather low number of patients needed to be excluded due to suboptimal image quality, which finally resulted in high-quality QFR analyses performed in 91.3% of real-world patients. This high percentage reflects the wide applicability of this novel resting coronary measure in patients undergoing coronary angiography.

The accuracy of QFR in identifying hemodynamic significance of coronary lesions as defined by an FFR of ≤0.80 has been demonstrated in the FAVOR (Functional Assessment by Various Flow Reconstructions) studies [10,14]. Our study confirmed the high diagnostic accuracy observed in the FAVOR studies in a large, real-world patient cohort, thereby supporting the use of QFR as a novel, less-invasive, adenosine-free tool for functional lesion interrogation in everyday clinical practice. Numerical differences in the diagnostic performance of QFR observed between studies may be related at least in part to the number of patients included and the different coronary artery disease severity observed, illustrated e. g. by a higher percentage of hemodynamic significant coronary lesions defined by FFR in the FAVOR studies [10,14]. Further, given that the diagnostic performance of QFR was lowest in patients with FFR values around the threshold, the distribution of values comes into play. When comparing non-hyperemic coronary indices, QFR had a better diagnostic performance as compared with resting Pd/Pa ratio. Hence, when relying on resting measures alone, superiority of QFR over resting Pd/Pa ratio is suggested. Resting Pd/Pa ratio is comparable to iFR, both numerically and with respect to the agreement with FFR [26]. Given that an iFR-guided revascularization strategy was shown to be prognostically non-inferior to FFR-guided revascularization, QFR may also be a useful measure to guide interventional therapy. Future studies are needed to delineate the non-inferiority of QFR analysis towards FFR assessment with respect to clinical outcomes. In line with previous studies [3,10,13], our analyses further demonstrated the limited ability of anatomic indices, albeit derived from 3D-QCA, in identifying functional lesion significance.

4.3. Limitations

A few limitations need to be considered. First, the study enrolling a large cohort of real-world patients undergoing FFR measurement for hemodynamic coronary lesion assessment is limited by the single center, post hoc design. The fact that patients with intermediate coronary lesions (40 to 70% diameter stenosis) were included in this analysis and FFR measurements were rather high in this patient cohort limits the generalizability of the results, and whether these observations also apply for patients with more severe disease remains to be determined. Second, optimal angiographic projections as recommended for QFR analyses were not always available, which may even have attenuated

Table 2
Diagnostic performance of quantitative flow ratio, resting Pd/Pa ratio, and anatomic indices.

Diagnostic performance (N = 516)	cQFR ≤0.80	fQFR ≤0.80	Pd/Pa ≤0.91	MLD ≤1.20	DS% ≥50%	AS% ≥58%
Diagnostic accuracy	93.4 (90.9–95.4)	91.9 (89.2–94.1)	84.3 (80.9–87.3)	78.9 (75.1–82.3)	80.4 (76.7–83.8)	63.2 (58.9–67.4)
Sensitivity (%)	75.0 (65.3–83.1)	72.0 (62.1–80.5)	62.0 (51.8–71.5)	25.0 (16.9–34.7)	34.0 (24.8–44.2)	71.0 (61.1–79.6)
Specificity (%)	97.8 (95.9–99.0)	96.6 (94.4–98.2)	89.7 (86.3–92.4)	91.8 (88.8–94.3)	91.6 (88.5–94.1)	61.3 (56.4–66.0)
PPV (%)	89.3 (81.2–94.1)	83.7 (75.2–89.7)	59.0 (51.1–66.6)	42.4 (31.5–54.0)	49.3 (39.0–59.6)	30.6 (27.0–34.4)
NPV (%)	94.2 (92.1–95.8)	93.5 (91.3–95.2)	90.8 (88.4–92.7)	83.6 (81.9–85.1)	85.2 (83.3–87.0)	89.8 (86.5–92.3)
(+)LR	34.7 (18.0–66.8)	21.4 (12.6–36.3)	6.0 (4.4–8.3)	3.1 (1.9–4.9)	4.0 (2.7–6.1)	1.8 (1.5–2.2)
(−)LR	0.26 (0.18–0.36)	0.29 (0.21–0.40)	0.4 (0.3–0.6)	0.8 (0.7–0.9)	0.7 (0.6–0.8)	0.5 (0.3–0.7)
AUC	0.86	0.84	0.76	0.58	0.63	0.66

Values are given as numbers and percentages with 95% confidence intervals. AS% = percent area stenosis, AUC = area under the receiver-operating characteristic curve, DS% = percent diameter stenosis.

the observed correlations. The strong correlations observed in this study when using high-quality coronary angiograms and FFR measurements performed in clinical routine, however, further support the wide applicability and feasibility of QFR in everyday clinical practice. Quantitative flow ratio may facilitate clinical decision making and guide coronary revascularization particularly in patients with tandem lesions, coronary bifurcations or multivessel coronary artery disease, which needs to be delineated in future studies.

5. Conclusion

This study demonstrates that QFR provides an adenosine-free diagnostic tool for functional lesion assessment with superior diagnostic accuracy as compared with resting Pd/Pa ratio and anatomic indices. Further, the applicability and feasibility of QFR in a large, real-world patient cohort was demonstrated. Hence, this non-hyperemic measure holds great potential for wide application in patients with intermediate coronary lesions. Future large-scale studies are required to assess whether QFR might obviate the need for hyperemia induction in selected patients and whether QFR-guided PCI translates into improved clinical outcomes.

Conflicts of interest

There are no conflicts of interest to declare.

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