Multimodality imaging in coronary artery disease: plaque characterization, computational haemodynamic simulation and risk stratification

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CHAPTER 4

Referral of patients for fractional flow reserve using quantitative flow ratio

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ABSTRACT

Aims: Quantitative flow ratio (QFR) is a recently developed technique to calculate fractional flow reserve (FFR) based on 3-dimensional quantitative coronary angiography and computational fluid dynamics, obviating the need for a pressure-wire and hyperaemia induction. QFR might be used to guide patient selection for FFR and subsequent percutaneous coronary intervention (PCI) referral in hospitals not capable to perform FFR and PCI. We aimed to investigate the feasibility to use QFR to appropriately select patients for FFR referral.

Methods and results: Patients who underwent invasive coronary angiography in a hospital where FFR and PCI could not be performed, and were referred to our hospital for invasive FFR measurement, were included. Angiogram images from the referring hospitals were retrospectively collected for QFR analysis. Based on QFR cut-off values of 0.77 and 0.86, our patient cohort was reclassified to "no referral" (QFR ≥0.86), referral for "FFR" (QFR 0.78-0.85) or "direct PCI" (QFR ≤0.77). In total, 290 patients were included. Overall accuracy of QFR to detect an invasive FFR of ≤0.80 was 86%. Based on a QFR cut-off value of 0.86, a 50% reduction in patient referral for FFR could be obtained, while only 5% of these patients had an invasive FFR of ≤0.80 (thus, these patients were incorrectly reclassified to the "no referral" group). Furthermore, 22% of the patients that still need to be referred could undergo direct PCI, based on a QFR cut-off value of 0.77.

Conclusion: QFR is feasible to use for the selection of patients for FFR referral.

Keywords: computational fluid dynamics; coronary artery disease; invasive imaging; quantitative coronary angiography

INTRODUCTION

Fractional flow reserve (FFR) is a technique to determine the hemodynamic significance of coronary artery stenoses during invasive coronary angiography (ICA).[1] FFR is commonly used to guide revascularization, as multiple studies have shown the superiority of FFR-based revascularization compared to angiography-based revascularization in patients with multivessel coronary artery disease.[2-7] Nevertheless, the widespread adoption of FFR is limited due to some important disadvantages, such as the need for a pressure-wire and hyperaemia induction.[8] Quantitative flow ratio (QFR) is a recently developed technique to calculate FFR.[9-12] QFR computation is based on 3-dimensional (3D) quantitative coronary angiography (QCA), for which only two invasive angiographic views of a coronary artery are required, and a flow-velocity component based on frame counting, followed by a simplified computational fluid dynamics approach. Recently, QFR was validated in a multicenter prospective study, using FFR as the reference standard, showing an overall diagnostic accuracy of 93% to detect an invasive FFR of ≤0.80.[11] Also, QFR showed a high diagnostic accuracy (90%) to detect ischemia on single-photon emission computed tomography myocardial perfusion imaging (SPECT MPI).[13]

QFR could be of important clinical value in hospitals not capable to perform FFR and percutaneous coronary intervention (PCI). Patients who undergo ICA in these hospitals need thereafter be referred to hospitals where PCI can be performed, when significant coronary artery disease is detected. Currently, the referral of these patients is based solely on angiographic assessment of coronary artery stenoses. This may lead to a significant rate of unnecessary referrals, because angiography is inaccurate in determining the hemodynamic significance of coronary artery stenoses.[14-16] As QFR is able to assess the hemodynamic significance with high diagnostic accuracy, this technique might be used to guide patient selection for FFR and subsequent PCI referral. Accordingly, the aim of the current study is to investigate 1) the feasibility to use QFR to appropriately select patients for FFR referral, and 2) the relationship between QFR and FFR in a large cohort of patients.

METHODS

Patients

Patients who underwent ICA in a hospital where FFR and PCI could not be performed, were referred to Leiden University Medical Center (The Netherlands) for invasive FFR measurement and PCI if needed, and were subsequently included in this analysis. Patients were excluded if 1) FFR was performed >6 months after ICA or 2) FFR was performed during hospitalization for myocardial infarction. Clinical data were prospectively entered in the electronic patient file and retrospectively analysed. The Medical Ethical Committee of the

Leiden University Medical Center, The Netherlands, approved this retrospective evaluation of clinically collected data and waived the need for written informed consent.

Invasive coronary angiography and fractional flow reserve

Mono- or biplane angiogram images from the referring hospitals were retrospectively collected for QFR analysis. In all patients, FFR was performed using a pressure-wire (Brightwire 2; Volcano Corp., San Diego, USA). FFR measurement was performed according to the manufacturer's guidelines. Standard 6F guiding catheters were used without side holes, slightly disengaged from the ostium, as they can impede flow. They were adequately flushed with saline to remove residual contrast medium. Proper anticoagulation (unfractionated heparin ≥50 U/kg) was administered. Calibration, equalization and measurements were subsequently properly carried out. Intracoronary nitrate (200 mcg) was administered prior to entering the coronary circulation. The sensor was advanced in principle 3 cm (minimum 2 if 3 cm was not feasible) distal to the lesion to be assessed, in order to have a freely rotating wire tip, avoiding the measurement of post-stenotic flow disturbances, flow eddies and pressure recovery phenomena. FFR was measured after induction of maximal hyperaemia by the administration of adenosine (140 mcg/kg/min) during ≥2 minutes in order to achieve a stable and steady-state maximal hyperaemia. Subsequently the pressure tracing encompassing the beginning of the hyperaemic and the recovery phase was recorded and the lowest FFR value was determined. Finally verification was performed by a pull back of the guidewire sensor to the catheter tip in order to verify equal pressures. If a drift larger than 3 mmHg was seen, re-equilizing took place and the FFR measurement was repeated until the drift was 3 mmHg or less. The exact anatomic position of the pressure-sensor at the angiogram was recorded and stored for all patients. Coronary artery stenoses with an invasive FFR of ≤0.80 were considered significant.

Quantitative flow ratio

QFR was calculated offline, using a dedicated software package (QAngio XA 3D/QFR, Medis medical imaging systems B.V., Leiden, The Netherlands). QFR was determined in all coronary arteries in which FFR was performed, at the location of the distal tip of the pressure-wire. Only coronary arteries (including side branches) with a quantitatively assessed diameter stenosis (DS) ≥1.4 mm were assessed. First, 2 angiographic views of a coronary artery were selected from the angiogram images of the referring hospital. Only angiographic views with projection angles ≥25° apart, containing a minimum of overlap and foreshortening of the coronary arteries, were included. Hereafter, a semi-automatic detection of the lumen contours was performed and a 3D model of the coronary artery was reconstructed. The proximal part of the left main coronary artery (LMCA) was excluded from the segmentation in the absence of coronary stenoses, based on the assumption that the loss of pressure in a normal coronary artery is negligible. However, in the presence of a stenosis in the LMCA,

the anatomical landmark that was used to indicate the start of the segmentation was placed proximal to this stenosis. The following QCA parameters were available for each coronary stenosis: DS, lesion length (LL), area stenosis (AS) and minimal lumen diameter (MLD). The Thrombolysis In Myocardial Infarction (TIMI) frame counting method was used to determine the contrast-flow velocity, which was based on the length of the coronary artery segment and the transport time of the contrast bolus. The angiographic view with the best image quality of the contrast medium was used for this purpose. Subsequently, the hyperaemic-flow velocity was calculated based on the contrast-flow velocity, and QFR was computed. Coronary arteries with 1) absence of angiographic views with projection angles ≥25° apart, 2) excessive overlap and/or foreshortening, 3) insufficient image quality or 4) a conduit segment or stent were excluded from the analysis. Coronary artery stenoses with a QFR of ≤0.80 were considered significant.

Statistical analysis

Distribution of continuous variables was determined using histograms and normal Q-Q plots. Continuous variables are presented as mean ± standard deviation if normally distributed and as median and 25-75% interquartile range (IQR) if non-normally distributed. Categorical variables are presented as number and percentages. The correlation and agreement between QFR and FFR were assessed with the Pearson's correlation coefficient and Bland-Altman plot respectively. Accuracy, sensitivity, specificity, positive and negative predictive value of QFR to detect an invasive FFR of ≤0.80 were determined and a receiver operating characteristic curve was constructed. To account for the possible presence of multiple included vessels per patient, a single observation was selected at random from that patient and the analysis carried out using the standard independent-samples assumption across patients. The analysis was then repeated multiple times for independent random choices to assess consistency of results. A sub-analysis was performed in patients only referred for FFR (i.e. without indication for PCI of another coronary artery by visual assessment) and with no coronary arteries excluded. In the prospective, multicenter FAVOR II Europe-Japan Study, QFR cut-off values of 0.86 and 0.77 yielded a sensitivity and specificity of >95% with FFR as the reference standard in a large cohort of patients.[17] Based on these QFR cut-off values, our patient cohort was reclassified to "no referral" (when QFR was ≥0.86) or "referral" (when QFR was <0.86) (Fig. 1). Moreover, patients reclassified to the "referral" group were further classified according to the QFR value to either performance of FFR (when QFR was between 0.78-0.85) or direct PCI (when QFR was ≤0.77). Subsequently, the number of true and false negatives in the "no referral" group, as well as the number of true and false positives in the "direct PCI" group, were assessed. All statistical analyses were performed with the SPSS software package (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) and MedCalc for Windows, version

18.2.1 (MedCalc Software, Ostend, Belgium). Statistical tests were considered significant if the P-value was <0.05.

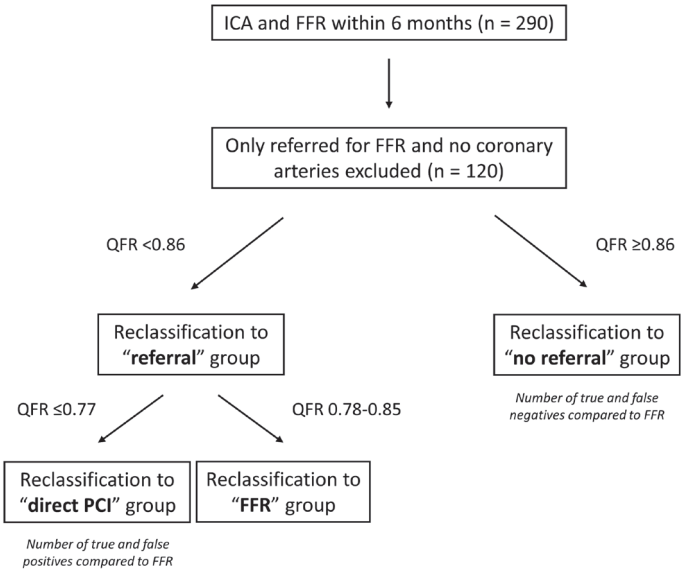

Fig. 1: Reclassification of patients according to QFR value. In total, 120 patients that were only referred for FFR and had no coronary arteries excluded, were included in the subanalysis. Patients were reclassified to "no referral" (when QFR was ≥0.86) or "referral" (when QFR was <0.86) based on the QFR value. Furthermore, patients reclassified to the "referral group" underwent further classification to either performance of FFR (when QFR was between 0.78-0.85) or direct PCI (when QFR was ≤0.77), according to the QFR value. FFR = fractional flow reserve; ICA = invasive coronary angiography; PCI = percutaneous coronary intervention; QFR = quantitative flow ratio.

RESULTS

Patients

In total, 290 patients who were referred for FFR were included in the study. Mean time between ICA and invasive FFR was 22.8 ± 25.1 days. The majority of patients included in our study (97%) underwent FFR measurement within 3 months after the initial ICA. The baseline characteristics of all patients are shown in Table 1. Mean age was 66.5 ± 9.4 years and 69.3% of the patients was male. 16.1% of the patients had a prior myocardial infarction and 34.7% had prior coronary revascularization (33.3% PCI and 2.4% coronary artery bypass grafting (CABG)).

Table 1: Baseline patient characteristics.

	Total (n = 290)
Age (years)	66.5 ± 9.4
Male, n (%)	201 (69.3%)
Hypertension, n (%)	208 (74.3%)
Diabetes, n (%)	67 (23.8%)
Obesity (BMI ≥30 kg/m^2)	64 (22.4%)
Prior MI, n (%)	46 (16.1%)
Prior PCI, n (%)	96 (33.3%)
Prior CABG, n (%)	7 (2.4%)

Values are mean ± SD or n (%).
BMI = body mass index; CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Relationship between QFR and FFR

In total, 386 coronary arteries were analysed. 52 (13.5%) coronary arteries were excluded due to insufficient image quality (n = 17), presence of a coronary stent (n = 4), excessive overlap and/or foreshortening of coronary arteries (n = 18), absence of angiographic views with projection angles ≥25° apart (n = 6), ostial stenosis (n = 5) or aneurysm (n = 2). QFR analysis was feasible in 225/243 (92.6%) left anterior descending coronary arteries (LAD), 33/52 (63.5%) right coronary arteries (RCA), 48/53 (90.6%) left circumflex coronary arteries (LCX) and 28/38 (73.7%) coronary side branches. Accordingly, 334 coronary arteries were included in the final analysis.

The included coronary arteries had a mean DS of 43.1 ± 8.5%, mean AS of 55.4 ± 12.9%, median LL of 20.0 mm (IQR 12.3-28.9 mm), mean MLD of 1.6 ± 0.3 mm and mean FFR of 0.85 ± 0.08 (Table 2). A good correlation (r = 0.81, P <0.001) and agreement (mean difference 0.010 ± 0.051) was found between QFR and invasive FFR (Fig. 2). Overall accuracy of QFR (cut-off value 0.80) to detect an invasive FFR of ≤0.80 was 86%, with a sensitivity, specificity, positive and negative predictive value of 70%, 92%, 77% and 89%, respectively. The area under the receiver operating characteristic curve for QFR to detect an invasive FFR of ≤0.80 was 0.92 (Fig. 3). We found no difference in calculated statistics across repeated analyses for different choices of included vessels in case multiple vessels per patient were included.

Table 2: Baseline vessel characteristics.

	Total (n = 334)
Analysed vessels	
Left anterior descending coronary artery, n (%)	225 (67.4%)
Left circumflex coronary artery, n (%)	48 (14.4%)
Right coronary artery, n (%)	33 (9.9%)
Coronary side branch, n (%)	28 (8.4%)
First diagonal branch, n (%)	9 (32%)
Second diagonal branch, n (%)	4 (14%)
Intermediate branch, n (%)	1 (4%)
Anterolateral branch, n (%)	6 (21%)
Obtuse marginal branch, n (%)	6 (21%)
Posterolateral circumflex branch, n (%)	2 (7%)
DS (%)	43.1 ± 8.5
LL (mm)	20.0 (12.3-28.9)
AS (%)	55.4 ± 12.9
MLD (mm)	1.6 ± 0.3
QFR	0.86 ± 0.09
FFR	0.85 ± 0.08

Values are mean ± SD or median (interquartile range).
AS = area stenosis; DS = diameter stenosis; FFR = fractional flow reserve; LL = lesion length; MLD = minimal lumen diameter; QFR = quantitative flow ratio.

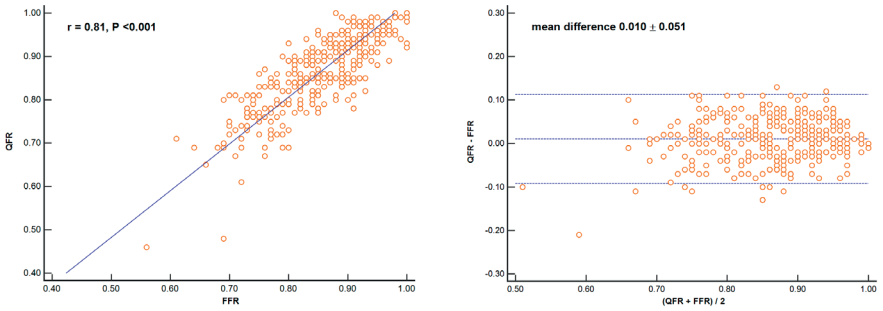

Fig. 2: Correlation and agreement between QFR (cut-off value 0.80) and invasive FFR (cut-off value 0.80). A good correlation (r = 0.81, P <0.001) and agreement (mean difference 0.010 ± 0.051) was found between QFR and invasive FFR. The 95% limits of agreement between QFR and FFR were -0.09 and 0.11. FFR = fractional flow reserve; QFR = quantitative flow ratio.

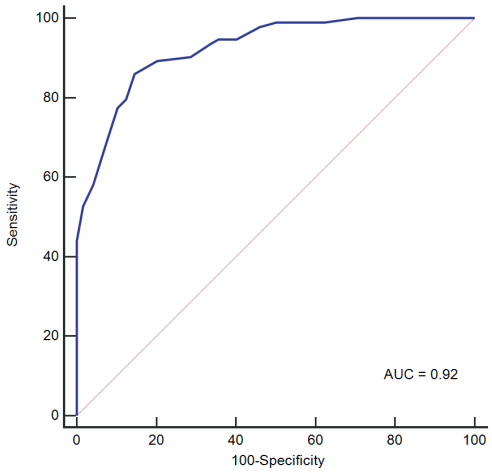

Fig. 3: Receiver operating characteristic curve for QFR to detect an invasive FFR of ≤0.80. The area under the receiver operating characteristic curve for QFR to detect an invasive FFR of ≤0.80 was 0.92. FFR = fractional flow reserve; QFR = quantitative flow ratio.

Feasibility of QFR to guide FFR referral

In total, 181 (54.2%) coronary arteries had a QFR value ≥0.86 and only 9 (5.0%) of these coronary arteries had an invasive FFR of ≤0.80 (Fig. 4). The invasive FFR and QFR values of these coronary arteries were in the range of 0.75-0.80 and 0.86-0.93, respectively.

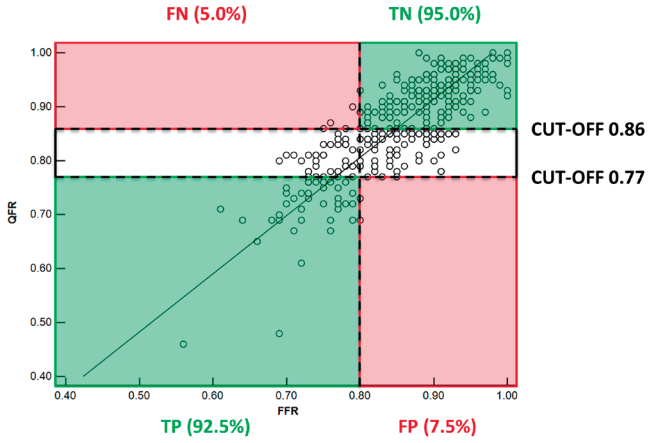

Fig. 4: True and false negative, and true and false positive results according to QFR cutoff values of 0.77 and 0.86. In total, 181 (54.2%) coronary arteries had a QFR value ≥0.86 and only 9 (5.0%) of these coronary arteries had an invasive FFR of ≤0.80. Furthermore, 53 (15.9%) coronary arteries had a QFR value ≤0.77 and only 4 (7.5%) of these coronary arteries had an invasive FFR of >0.80. FFR = fractional flow reserve; FN = false negative; FP = false positive; QFR = quantitative flow ratio; TN = true negative; TP = true positive.

Furthermore, 53 (15.9%) coronary arteries had a QFR value ≤0.77 and only 4 (7.5%) of these coronary arteries had an invasive FFR of >0.80. The invasive FFR values of these coronary arteries were in the range of 0.81-0.85 and the QFR values were 0.77. Subsequently, the QFR cut-off values of 0.77 and 0.86, which were derived from the FAVOR II Europe-Japan Study, were used in patients who were only referred for FFR (without indication for PCI of another coronary artery) and had no coronary arteries excluded from the analysis (n = 120). Based on a cut-off value for QFR of 0.86, 60 (50%) patients could be reclassified to the "no referral" group, with only 3 patients having an invasive FFR of ≤0.80 (thus, these patients were incorrectly reclassified to the "no referral" group) (Table 3). The invasive FFR and QFR values in these patients were in the range of 0.79-0.80 and 0.86-0.93, respectively. Based on a QFR cut-off value of 0.77, 13 (11%) patients could be reclassified to the "direct PCI" group, with only 2 patients having an invasive FFR >0.80 (thus, these patients were incorrectly reclassified to the "direct PCI" group). The invasive FFR values in these patients were 0.83 and 0.85 and the QFR values were 0.77. Of the 47 (39%) patients that would still need to undergo FFR, 28 had an invasive FFR of >0.80 and 19 had an invasive FFR ≤0.80. In Fig. 5, an example of a patient is shown who could be deferred from FFR referral according to the QFR value. In Fig. 6, an example of a patient is displayed that could be referred for direct PCI according to the QFR value.

Table 3: Patient referral for FFR and PCI using QFR cut-off values of 0.77 and 0.86.

		FFR		**Total**
		>0.80 (negative)	**≤0.80** (positive)	
QFR	**≥0.86** (no referral)	57	3	60
	0.78-0.85 (FFR)	28	19	47
	≤0.77 (direct PCI)	2	11	13
Total		87	33	120

FFR = fractional flow reserve; PCI = percutaneous coronary intervention; QFR = quantitative flow ratio.

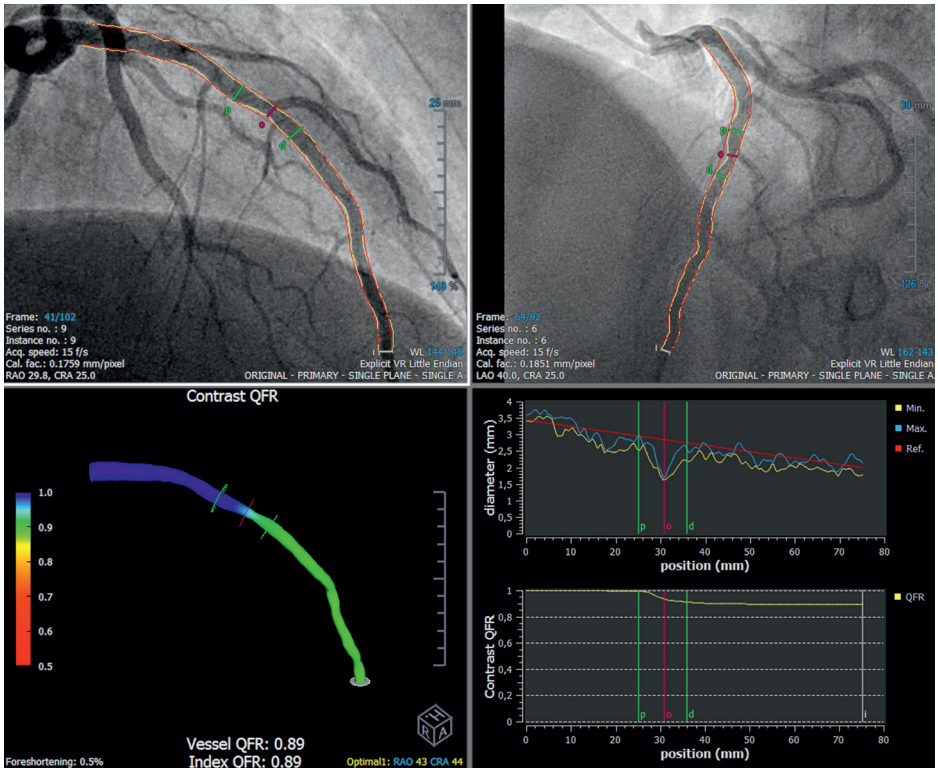

Fig. 5: Example of a patient who could be deferred from FFR referral according to the QFR value. Example of a left anterior descending coronary artery with a QFR of 0.89.
According to a cut-off value of QFR of 0.86, this patient could be deferred from FFR referral.
The invasive FFR measured at the same location was 0.86. FFR = fractional flow reserve; QFR = quantitative flow ratio.

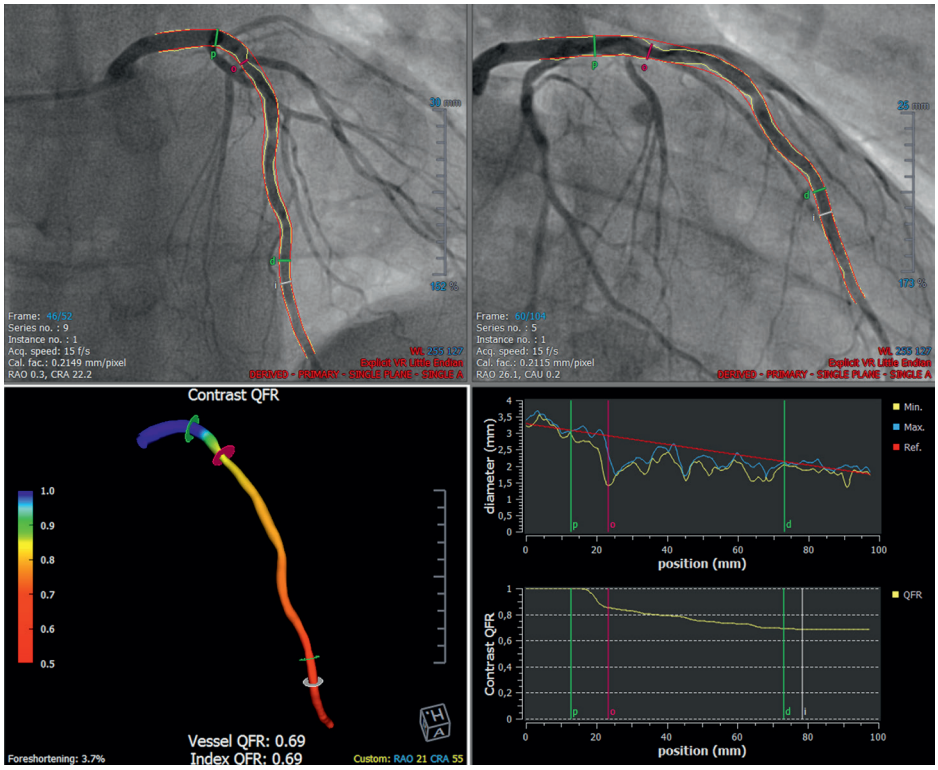

Fig. 6: Example of a patient who could be referred for direct PCI according to the QFR value. Example of a left anterior descending coronary artery with a QFR of 0.69. According to a cut-off value of QFR of 0.77, this patient could be referred for direct PCI. The invasive FFR measured at the same location was 0.73. FFR = fractional flow reserve; PCI = percutaneous coronary intervention; QFR = quantitative flow ratio.

DISCUSSION

In this study, QFR showed a good correlation and agreement with invasive FFR and had a diagnostic accuracy of 86% for the detection of an invasive FFR of ≤0.80. Based on a QFR cut-off value of 0.86, a 50% reduction in patient referral for FFR could be obtained, while only 5% of these patients had an invasive FFR of ≤0.80. Furthermore, 22% of the patients that still need to be referred could undergo direct PCI, based on a QFR cut-off value of 0.77.

Diagnostic accuracy and reproducibility of QFR

In our study, QFR showed a high diagnostic accuracy for the identification of an invasive FFR of ≤0.80 in a large cohort of patients. Recently, several studies have been performed comparing QFR with invasive FFR as the reference standard. In the prospective multicenter FAVOR Pilot Study, QFR and invasive FFR were compared in 84 coronary arteries from

73 patients with intermediate coronary stenoses (defined as DS 30-80% by visual assessment).[10] A good correlation (r = 0.77, P <0.001) and agreement (mean difference 0.001 ± 0.059) were observed between QFR and invasive FFR. Diagnostic accuracy, sensitivity, specificity, positive and negative predictive value of QFR to detect an invasive FFR of ≤0.80 were 85%, 74%, 91%, 83% and 86%, respectively. The multicenter FAVOR II China Study assessed the diagnostic accuracy of QFR online in the catheterization laboratory prior to FFR measurement.[11] A total of 328 coronary arteries from 308 patients with intermediate coronary stenoses (defined as DS 30-90% by visual estimation) were prospectively and consecutively included. Diagnostic accuracy to identify an invasive FFR of ≤0.80 was considerably higher for QFR compared to DS ≥50% assessed by QCA (92.7% vs. 59.6%, P <0.001). Sensitivity, specificity, positive and negative predictive value of QFR were 94.6%, 91.7%, 85.5% and 97.1%, respectively. The FAVOR II Europe-Japan Study assessed the diagnostic accuracy of QFR online in 317 vessels from 272 patients with intermediate coronary stenoses (defined as DS 30-90% by visual estimation).[17] Using invasive FFR as the reference standard, diagnostic accuracy of QFR was 87% with a sensitivity, specificity, positive and negative predictive value of 87%, 87%, 76% and 93%, respectively. In the WIFI II Study, QFR was compared with invasive FFR in 240 coronary vessels of 172 patients.[18] In this study, a good correlation (r = 0.70, P <0.001) and agreement (mean difference 0.01 ± 0.08) were observed between QFR and invasive FFR. Furthermore, diagnostic accuracy, sensitivity, specificity, positive and negative predictive value of QFR were 83%, 77%, 86%, 75% and 87%, respectively. Finally, a retrospective study was performed in 151 coronary arteries from 142 patients who underwent ICA and subsequent FFR measurement.[19] QFR showed a good correlation (r = 0.80, P <0.001) and agreement (mean difference 0.01 ± 0.05) with invasive FFR. Diagnostic accuracy, sensitivity, specificity, positive and negative predictive value of QFR were 88.7%, 89.1%, 88.6%, 77.4% and 94.9%, respectively.

The reproducibility of QFR has been assessed in multiple studies. It was recently shown by Chang et al. that QFR has a good reproducibility to assess the hemodynamic significance of CAD, when performed by two independent core laboratories (mean difference in QFR 0.004 ± 0.03).[20] Moreover, Westra et al. noted a good correlation (r = 0.83, P <0.001) and agreement (-0.03 ± 0.07) between QFR that was assessed during ICA (online) and afterwards by a separate core laboratory (offline).[17] Also, the authors found no significant difference between the diagnostic performance of online and offline QFR assessment (0.91 vs. 0.87, P = 0.09). Finally, van Rosendael et al. demonstrated a good agreement of QFR values between two independent observers in a small prospective study (mean difference in QFR 0.02 ± 0.04).[12]

Clinical applicability of QFR

According to the European Society of Cardiology (ESC) guidelines, FFR is recommended to identify hemodynamically significant coronary lesions in stable patients when evidence of myocardial ischemia is not available.[6, 7] Nevertheless, the widespread clinical adoption of FFR is limited because of the need for hyperaemia induction and the use of a pressure-wire.[8] Hyperaemia induction may lead to significant patient symptoms (e.g. shortness of breath, chest discomfort) and prolongation of the procedural time, whereas the use of a pressure-wire is costly and can be difficult in tortuous coronary arteries. Moreover, invasive FFR measurements may be suboptimal due to waveform artifacts or signal drift.[21] QFR is a newly developed technique to calculate FFR, based on 3D QCA and computational fluid dynamics. As opposed to invasive FFR, QFR computation does not require hyperaemia induction or the use of a pressure-wire. QFR is also highly feasible to use in the catheterization laboratory during ICA, with a mean QFR computational time of only 4.36 ± 2.55 minutes when performed by a dedicated technician.[11] QFR could be of important clinical use in hospitals that are not capable to perform FFR and PCI. At present, these hospitals perform a visual assessment of the severity of coronary stenoses or additional functional testing (either before or after ICA) to decide whether a patient should be referred to a hospital for FFR and subsequent PCI. However, visual assessment alone is known to be inaccurate in determining the hemodynamic significance of coronary artery stenoses.[14-16] Moreover, additional functional testing is time-consuming and may lead to increased radiation exposure, depending on the functional test used. A proper selection of patients for FFR referral is important, as the performance of a second ICA with FFR measurement is costly and may lead to major procedural complications. The use of QFR could significantly extend the possibility to perform functional assessment of coronary artery stenoses to a wide range of hospitals.

According to the current study, FFR referral based on QFR enables the deferral of a second ICA in a large subset of patients. Our study showed that a 50% reduction in patient referral for FFR could be obtained, based on a QFR cut-off value of 0.86. Only 5% of these patients would incorrectly be deferred from FFR referral based on QFR. Furthermore, 22% of the patients that still need to be referred could undergo direct PCI, based on a QFR cut-off value of 0.77.

LIMITATIONS

This study was limited by its retrospective character. A substantial part of the coronary arteries (13.5%) was excluded due to suboptimal angiographic projections. The acquisition guide, which is included in the QFR software package, enables the selection of optimal angiographic projections with a minimum of vessel overlap and/or foreshortening.

Prospective, in-procedure use of this acquisition guide in the catheterisation laboratory would probably lead to a smaller amount of excluded coronary arteries. Moreover, lumen contour detection would be more accurate when performed on prospectively selected angiographic projections with high image quality. Accordingly, use of the acquisition guide for the selection of angiographic images may result in a superior diagnostic accuracy of QFR and a further increase in the proportion of patients that could be correctly deferred from FFR referral. Although the coronary lesions included in our study could be considered relatively mild and low-risk, the baseline vessel characteristics were comparable to that observed in the FAVOR II studies. Also, our patient cohort is a real-world representation of the patients that are currently referred for FFR according to the guidelines. Finally, because of the retrospective design of this study, selection bias cannot be excluded.

CONCLUSIONS

QFR showed a good relationship with invasive FFR in a large cohort of patients. Also, QFR was feasible to select patients for FFR referral. Based on a QFR cut-off value of 0.86, FFR referral could be reduced by 50%. Only 5% of the patients would incorrectly be deferred from FFR referral based on the QFR value. Moreover, 22% of the patients that still need to be referred could undergo direct PCI, based on a QFR cut-off value of 0.77. Future studies need to be performed in hospitals without FFR and PCI facilities to prospectively determine the feasibility of FFR referral, based on QFR. Furthermore, large-scale randomized outcome studies are required before QFR could be implemented in clinical practice as a definite alternative to invasive FFR.

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