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ORIGINAL ARTICLE
Interventional cardiology and cardiac surgery

Prognostic role of discordance between quantitative flow ratio and visual estimation in revascularization guidance

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Aims Revascularization guided by functional severity has presented improved outcomes compared with visual angiographic guidance. Quantitative flow ratio (QFR) is a reliable angiography-based method for functional assessment. We sought to investigate the prognostic value of discordance between QFR and visual estimation in coronary revascularization guidance.

Methods and results We performed offline QFR analysis on all-comers undergoing coronary angiography. Vessels with calculated QFR were divided into four groups based on the decision to perform or defer percutaneous coronary intervention (PCI) and on the QFR result, i.e.: Group A (PCI–, QFR > 0.8); Group B (PCI+, QFR ≤ 0.8); Group C (PCI+, QFR > 0.8); Group D (PCI–, QFR ≤ 0.8). Patients with at least one vessel falling within the disagreement groups formed the discordance group, whereas the remaining patients formed the concordance group. The primary endpoint was the composite endpoint of cardiovascular death, myocardial infarction, and ischaemia-driven revascularization. Overall, 546 patients were included in the study. Discordance between QFR and visual estimation was found in 26.2% of patients. After a median follow-up period of 2.5 years, the discordance group had a significantly higher rate of the composite outcome (hazard ratio: 3.34, 95% confidence interval 1.99–5.60, $P < 0.001$). Both disagreement vessel Groups C and D were associated with increased cardiovascular risk compared with agreement Groups A and B.

Conclusion Discordance between QFR and visual estimation in revascularization guidance was associated with a worse long-term prognosis. Our results highlight the importance of proper patient selection for intervention and the need to avoid improper stent implantations when not dictated by a comprehensive functional assessment.

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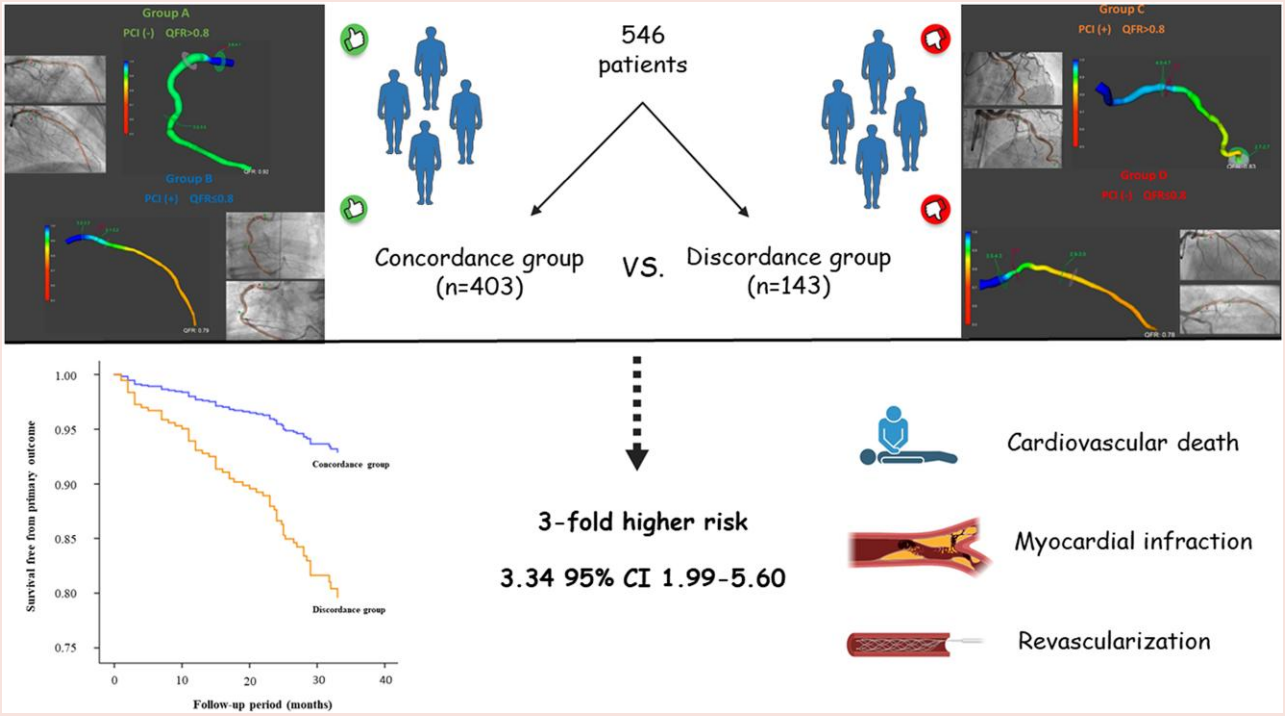
Graphical Abstract



Keywords Quantitative flow ratio • Fractional flow reserve • Percutaneous coronary intervention • Prognosis • Coronary angiography

Translational perspective

Disagreement between quantitative flow ratio and visual estimation in revascularization guidance is a risk factor for adverse cardiovascular events. Quantitative flow ratio guidance in revascularization could prevent unnecessary interventions and indicate necessary revascularization procedures, improving clinical outcomes.

Introduction

Haemodynamic significance of coronary stenosis has been identified as a reliable index in revascularization guidance. Visual estimation by plain coronary angiography cannot accurately predict the functional severity of coronary lesions.[1] Fractional flow reserve (FFR) has been introduced as the gold standard for functional interrogation of coronary stenosis leading to fewer major cardiovascular adverse events (MACEs) compared with visual angiographic guidance.[2–4] Although adopting FFR-guided revascularization in clinical practice could prevent unnecessary interventions or suspension of necessary revascularization procedures, real-word data show a systematic underutilization of the method.[5] Reduced implementation of FFR has been mainly attributed to the increased operational time and cost, the requirement of an extra pressure wire and technical aspects as well, such as pressure wire drift and damping.

Several angiography-derived FFR indices have been developed to overcome invasive FFR drawbacks.[6] Quantitative flow ratio (QFR) is a well-studied method of FFR estimation by angiographic views using firstly a reconstructed three-dimensional (3D) anatomic model of the coronary vessel of interest and secondly fluid dynamics computation, without requiring the instrumentation of the coronary artery.[7] This novel method has consistently presented high diagnostic performance and good correlation with the gold standard FFR[8] and has also been used in microvascular dysfunction assessment.[9,10] Recently, QFR demonstrated encouraging results regarding clinical outcomes. The results of the randomized FAVOR III China trial reported that QFR-guided revascularization was associated with improved 1- and 2-year clinical outcomes compared with plain coronary angiography-guided revascularization.[11–13] We sought to investigate the prevalence and the prognostic role of discordance between QFR and plain coronary angiography in revascularization guidance for all-comers at both patient and vessel levels.

Methods

Study design

Patients with coronary artery disease who were prospectively enrolled in a large cohort assessing eligibility for proprotein convertase subtilisin–kexin Type 9 inhibitor treatment[14] and underwent coronary angiography in 'Hippokration' General Hospital between October 2018 and December 2019 were considered for enrolment in this study. Patients referred for coronary artery bypass graft (CABG) surgery after coronary angiography were excluded from this analysis. We aimed to measure QFR in all vessels in each patient. Patients with at least one vessel satisfying the technical requirements for QFR measurement from image acquisition during the coronary angiography were included. All vessels with calculated QFR were divided into four groups based on whether percutaneous coronary intervention (PCI) was performed or deferred and on the other hand, on the QFR result with a cut-off point ≤0.8 indicating functionally significant ischaemia and thus need for revascularization, i.e.: Group A, where PCI was not performed and QFR was indicative of non-significant stenosis (PCI−, QFR > 0.8); Group B, where PCI was performed and QFR result was indicative of significant stenosis (PCI+, QFR ≤ 0.8); Group C, where PCI was performed while QFR was indicative of non-significant stenosis (PCI+, QFR > 0.8); Group D, where PCI was not performed while QFR was indicative of significant stenosis (PCI−, QFR ≤ 0.8). Groups A and B represent agreement between QFR and visual estimation regarding revascularization guidance, whereas Groups C and D represent disagreement between the two methods. Patients with at least one vessel falling within Group C or D formed the discordance group, whereas the remaining patients formed the concordance group.

Demographic data, cardiovascular risk factors, indications for coronary angiography, and procedural data were collected from the medical records of the study centre. Follow-up was organized by outpatient clinic visits, medical records, or telephone calls.

This study was conducted in accordance with the declaration, and the study protocol was approved by the institutional review board of the Hippokration General Hospital. All patients provided written informed consent.

Study population

Patients ≥18 years of age who underwent coronary angiography for any indication were eligible for inclusion in the study. Exclusion criteria were: (i) referral for CABG after coronary angiography and (ii) absence of at least one vessel satisfying the technical requirements for QFR measurement. Requirements for calculating QFR are defined by software guidelines as follows: (i) two optimal projections at least 25° apart; (ii) absence of excessive vessel overlap; (iii) absence of excessive foreshortening; (iv) adequate end-diastolic vessel opacification; (v) vessel >2 mm in diameter; (vi) lesion >3 mm from aorta; and (vii) absence of a bypass graft.

Coronary angiography and quantitative flow ratio computation

Conventional coronary angiography and PCI were performed according to best local practice. The calculation of QFR was performed offline using the software package QAngio XA 3D (Medis, Medical Imaging, Leiden, The Netherlands). Contrast QFR was utilized in the present analysis, as a reliable and simpler method.[15] Quantitative flow ratio analysis was performed by two validated operators, blinded to the visual estimation of the interventional cardiologist and the decision to perform or to defer PCI. In case computation of QFR was not feasible in a vessel the reason was reported.

Endpoints

The primary endpoint was the composite of cardiovascular death, myocardial infarction (MI), and ischaemia-driven revascularization. At vessel level, the secondary endpoint was the vessel-oriented composite endpoint (VOCE), defined as the composite of vessel-related cardiovascular death, vessel-related MI, and ischaemia-driven revascularization. Cardiovascular adverse events were monitored mainly by telephone calls and less frequently by outpatient visits due to COVID-19 pandemic. When an adverse event was reported, the investigators would review the medical records of the institution where each patient was being hospitalized (in most cases, the study centre was involved). In case of sudden cardiac death before the patient was admitted to a hospital, the event was classified as cardiovascular death. Cardiovascular death in patients with multiple treated vessels or vessels with untreated lesions was assigned to each vessel. Myocardial infarction was diagnosed according to the fourth universal definition.[16] In case of MI without a definite culprit vessel, each vessel with treated or untreated lesion was regarded as culprit. Ischaemia-driven revascularization was defined as any revascularization (PCI or CABG) in the presence of angina and/or abnormal results of non-invasive functional diagnostic tests. In case of multiple adverse events regarding the same vessel or patient, the first occurred was the one reported.

Statistical analysis

Based on the hypothesis that patients with untreated lesions and calculated QFR ≤ 0.8 (Group D) have a two-fold increased risk of presenting the primary endpoint in a 2-year follow-up period compared with patients with untreated lesions and QFR > 0.8 (Group B), we calculated the sample size at 250 subjects for Group B and 25 subjects for Group D with 80% power and 0.05 statistical level.[17] Categorical variables were presented as numbers and percentages, and continuous variables were presented as means ± standard deviations or medians with an interquartile range depending on their distribution. Student's *t*-test or the Mann–Whitney *U* test was used for comparing continuous variables, and χ^2 test was used for categorical variables. Logistic regression was used to estimate odds ratios and 95% confidence intervals (CIs). Multivariate Cox regression analysis was used to estimate hazard ratios (HRs) and 95% CIs. The prognostic effect of the different subgroups on the vessel-oriented composite outcome was evaluated also by mixed logistic regression models (clustered by patient level).

Results

Patient and vessel characteristics

Initially, 1346 patients were screened for inclusion, 546 of whom were eventually included in the study. The most common reason for exclusion was the lack of calibration data (*Figure 1*). Baseline patient and procedural characteristics are displayed in *Table 1*. The mean age was 65 (±11) years and 79% of patients were male. Chronic coronary syndrome was the indication for coronary angiography in the majority of the cohort (63%). The discordance group (visual-functional mismatch in at least one vessel) consisted of 143 patients (26.2%), whereas 403 patients (73.8%) were classified into concordance group. The baseline characteristics of patients in concordance group were mostly comparable with baseline characteristics of patients in discordance group. However, patients in discordance group were older, with more extended coronary artery disease and a higher SYNTAX score (*Table 1*). Overall, QFR was calculated in 1185 vessels (72.2% of total vessels). Right coronary artery was more often involved in cases of inability to calculate QFR, and the most common restriction for computing QFR was the absence of appropriate projections in ∼40% of total missing cases (see Supplementary material online, *Table S1*). The inter-observer reliability in calculating QFR between the two investigators was high (intra-class correlation coefficient = 0.92, 95% CI 0.82–0.97).

Vessel groups

Agreement between QFR and visual estimation regarding revascularization guidance (Groups A and B) was observed in 1010 vessels (85.2%), whereas disagreement between the two methods (Groups C and D) was present in 175 vessels (14.8%). In specific, Group A (PCI−, QFR > 0.8), Group B (PCI+, QFR ≤ 0.8), Group C (PCI+, QFR > 0.8), and Group D (PCI−, QFR ≤ 0.8) included 757 (63.9%), 253 (21.3%), 79 (6.7%), and 96 (8.1%) vessels, respectively (*Figure 2*).

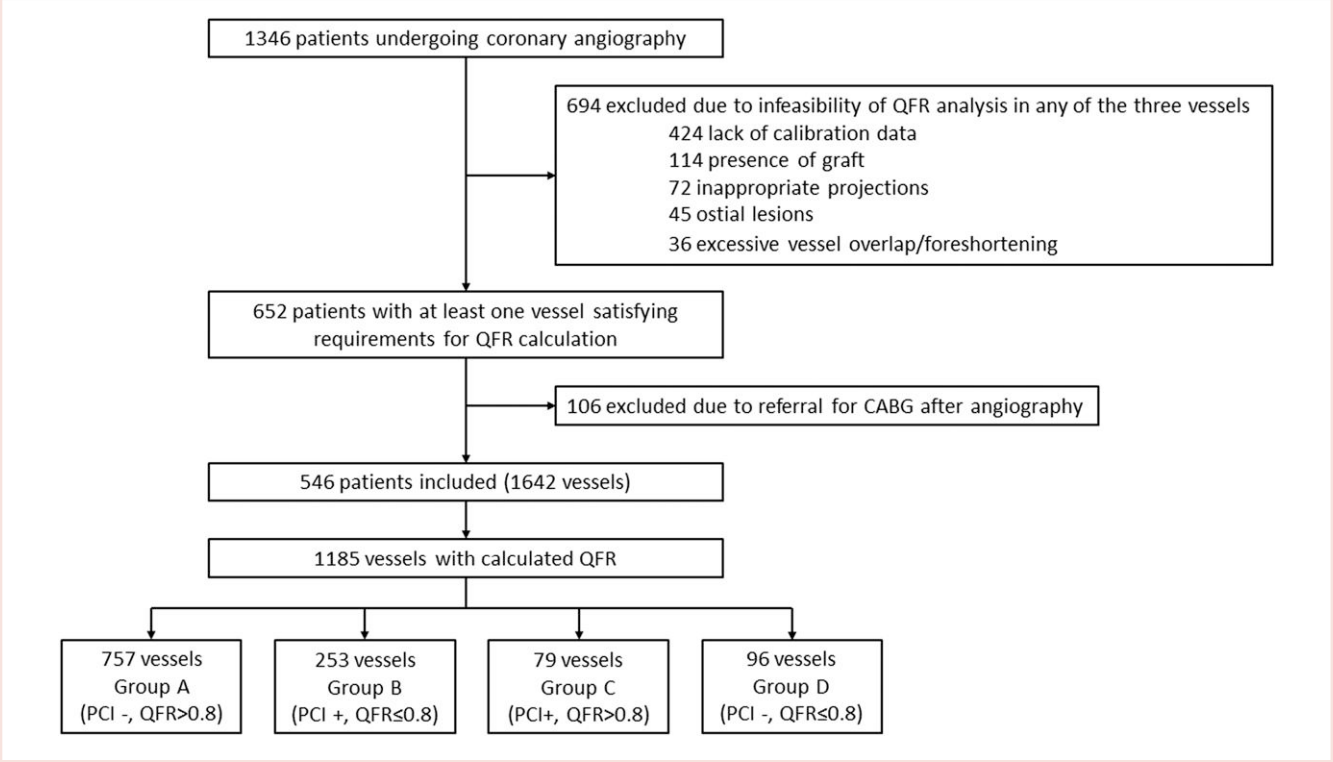


Figure 1 Flow chart of the study. CABG, coronary artery by-pass; PCI, percutaneous coronary intervention; QFR, quantitative flow ratio.

Endpoints

The median follow-up period was 30.5 (interquartile range: 26.4–33.7) months. Multivariate regression analysis showed a significant higher rate of the primary composite outcome of cardiovascular death, MI, and ischaemia-driven revascularization in the discordance group compared with concordance group (23.4 vs. 6.9%, HR: 3.34, 95% CI 1.99–5.60, $P < 0.001$; *Figure 3*). The higher risk in discordance group was driven by ischaemia-driven revascularization and cardiovascular death (HR: 3.69, 95% CI 1.80–7.30, $P < 0.001$ and HR: 3.52, 95% CI 1.43–7.59, $P = 0.001$, respectively). Rates of MI were also numerically increased compared with concordance group, although statistical significance was not reached (HR: 1.99, 95% CI 0.73–5.25, $P = 0.170$; *Table 2*). Estimates were adjusted for sex, age, chronic kidney disease, heart failure, diabetes mellitus, extent of coronary artery disease, and SYNTAX score. A history of heart failure and chronic kidney failure were independent risk factors for presenting the primary endpoint. Subgroup analysis revealed that the increased cardiovascular risk in cases of discordance between QFR and angiographic estimation was consistent in both patients with chronic coronary syndrome and patients with acute coronary syndrome (HR: 3.47, 95% CI 1.51–7.99, $P = 0.003$ and HR: 3.35, 95% CI 1.70–6.60, $P < 0.001$, respectively). Of note, when staged PCI was planned after the index procedure, the patient was classified in concordance group if QFR ≤ 0.80 in relative vessel and in discordance group if QFR > 0.80 in relative vessel.

At vessel level, VOCE was observed in 16 (2.1%), 19 (7.5%), 11 (13.9%), and 19 (19.8%) vessels in Groups A–D, respectively. After adjustment for covariates, vessels in disagreement Groups C and D were associated with a significant higher risk of cardiovascular adverse events compared with agreement Groups A and B. Compared with the lowest risk Group A (PCI–, QFR > 0.8), the HR for Group B (PCI+, QFR ≤ 0.8), Group C (PCI+, QFR > 0.8), and Group D (PCI–, QFR ≤ 0.8) were 2.44 (95% CI 1.23–4.82), 5.69 (95% CI 2.60–12.4), and 7.05 (95% CI 3.57–13.9), respectively, with Group D presenting the higher risk of VOCE among the four groups (*Figure 4*). Compared with the agreement Group B where PCI was performed, disagreement Groups C and D presented a two- and a three-fold higher risk of VOCEs, respectively (HR: 2.38, 95% CI 1.12–5.05 and HR: 3.02, 95% CI 1.59–5.74, respectively).

Discussion

To the best of our knowledge, this was the first real-world cohort of all-comers undergoing coronary angiography with the longest follow-up to assess the level of agreement between visual estimation and QFR regarding revascularization guidance and to estimate its prognostic value. The main findings of this QFR analysis are: (i) discordance between QFR and angiographic estimation was relatively high, accounting for 26.2% of patients at patient level and 14.8% of total vessels at vessel level; (ii) disagreement between QFR and angiographic estimation in revascularization guidance was an independent prognostic factor of increased adverse cardiovascular events; (iii) deferring treatment of haemodynamically significant lesions according to QFR was associated with the highest rate of VOCE compared with the remaining groups; (iv) treating a functionally insignificant lesion was also related with worse prognosis compared with agreement groups.

Although several methods of angiography-based FFR estimation have emerged, we used QFR due to various advantages against the remaining indices.[7] Firstly, QFR is supported by the largest amount of evidence, having been tested among special populations such as patients with microvascular dysfunction, diabetes, chronic kidney disease, and aortic stenosis and in special conditions such as the acute phase of ST-elevation myocardial infraction (STEMI) and in-stent restenosis. The prognostic role of QFR has also been evaluated in both randomized and retrospective studies. Additionally, the use of thrombolysis in

Table 1 Patients' baseline characteristics

	Overall ($n = 546$)	Concordance ($n = 403$)	Discordance ($n = 143$)	*P*-value
Clinical				
Age, mean (SD)	65 (11)	64 (10.9)	66 (11)	0.040
Male, *n* (%)	433 (79.3)	313 (77.7)	120 (83.9)	0.145
Diabetes mellitus, *n* (%)	148 (27.1)	102 (25.3)	46 (32.2)	0.132
Hypertension, *n* (%)	371 (67.9)	266 (66)	105 (80)	0.147
Dyslipidaemia, *n* (%)	439 (80,4)	325 (80.6)	114 (66.9)	0.638
Smoking, *n* (%)	389 (71.2)	288 (71.5)	101 (70.6)	0.711
Chronic kidney disease, *n* (%)	75 (13.7)	50 (12.4)	25 (17.5)	0.143
Stroke, *n* (%)	33 (6)	24 (6)	9 (6.3)	0.908
Peripheral artery disease, *n* (%)	24 (4.4)	15 (3.7)	9 (6.3)	0.208
Heart failure, *n* (%)	62 (11.4)	47 (11.7)	15 (10.5)	0.674
Atrial fibrillation, *n* (%)	38 (7)	27 (6.7)	11 (7.7)	0.713
CAD, *n* (%)	167 (30.6)	115 (28.5)	51 (35.6)	0.131
Previous PCI, *n* (%)	118 (21.6)	83 (20.6)	35 (24.5)	0.366
Previous CABG, *n* (%)	6 (1.1)	5 (1.2)	1 (0.7)	0.586
LVEF %, median (IQR)	50 (45–55)	50 (45–55)	50 (45–55)	0.197
SYNTAX score, median (IQR)	12 (5–19)	11 (5–18)	15 (7–19)	0.020
Presentation				0.697
STEMI, *n* (%)	104 (18.8)	81 (20)	23 (15.9)	
NSTEMI, *n* (%)	75 (14.2)	54 (13.4)	21 (14.7)	
Unstable angina, *n* (%)	23 (4.2)	17 (4.2)	6 (4.1)	
CCS, *n* (%)	344 (62.7)	251 (62.1)	93 (64.1)	
CAD extent				0.010
None, *n* (%)	85 (15.5)	68 (16.8)	17 (11.7)	
1 vessel, *n* (%)	218 (39.9)	175 (43.3)	43 (30)	
2 vessels, *n* (%)	152 (27.8)	101 (25)	41 (28.7)	
3 vessels, *n* (%)	88 (16)	53 (13.1)	35 (24.1)	
Procedural				
Radial access, *n* (%)	397 (72.7)	290 (71.8)	107 (74.8)	0.290
Total stent length, median (IQR)	20 (0–38)	20 (0–40)	20 (0–38)	0.656

CABG, coronary artery bypass graft; CAD, coronary artery disease; CCS, chronic coronary syndrome; IQR, interquartile range; LVEF, left ventricle ejection fraction; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; STEMI, ST-elevation myocardial infarction.

myocardial infraction frame count method offers a more patient-specific estimation of flow velocity. In the present study, offline measurement of QFR was feasible in 72.2% of the total vessels included in the study. In previous studies with retrospective analysis, successful QFR analysis ranged from 59.2 to 89.7%.[18–23] As in our study, in many retrospective studies, the lack of two appropriate projections was the most common reason for the unfeasibility to calculate QFR.[8,18,20] Excessive vessel overlap[21,22] and lack of calibration data[19,23] have also been reported as major restrictions in offline QFR measurement. Lack of calibration data was part of the exclusive criteria at the initial screening in our study (*Figure 1*). These issues are much less of a problem when patients are investigated prospectively, and thus, the application of the technique in the cath lab routine could provide a useful ally in guiding treatment.

Discordance in revascularization guidance between QFR and estimation by plain coronary angiography was found in a significant proportion of the cohort. At patient level, mismatch between the methods was present in 26.2% of patients. In another study of similar design to our analysis, Zhang *et al.*[23] reported disagreement between QFR and coronary angiography in 41.6% of the cohort. In line with our results, patients in the discordance group were older and more likely to have extended coronary artery disease and higher SYNTAX score.[23] At vessel level, mismatch was present in 14.8% of total vessels. Disagreement groups included a similar number of cases, with Group C (PCI+, QFR > 0.8) representing 6.7% of total vessels and Group D (PCI−, QFR ≤ 0.8) representing 8.1% of total vessels. In a study by Sugiyama *et al.*[24] investigating the determinants of visual-functional discordance, the disagreement between the two methods was found in 35.6% of the total vessels. The lower rate of visual-functional discordance in our study at both patient and vessel levels compared with the studies mentioned above could be explained by an overestimation of Group A (PCI−, QFR > 0.8) in our cohort. In contrast to the other investigators, we included vessels with minimal coronary artery disease (lesion <30%), overestimating the agreement between QFR and visual estimation. However, the analysis of an all-comers to the cath lab study cohort, such as in our study, increases the generalizability of our results in a real-life, everyday clinical practice.

In our study, after a long follow-up of more than 2.5 years, patients in the discordance group had a three-fold higher risk to present the primary composite outcome of cardiovascular death, MI, and ischaemia-driven revascularization. In the same line, Zhang *et al.*[23] showed that patients with a revascularization plan inconsistent to

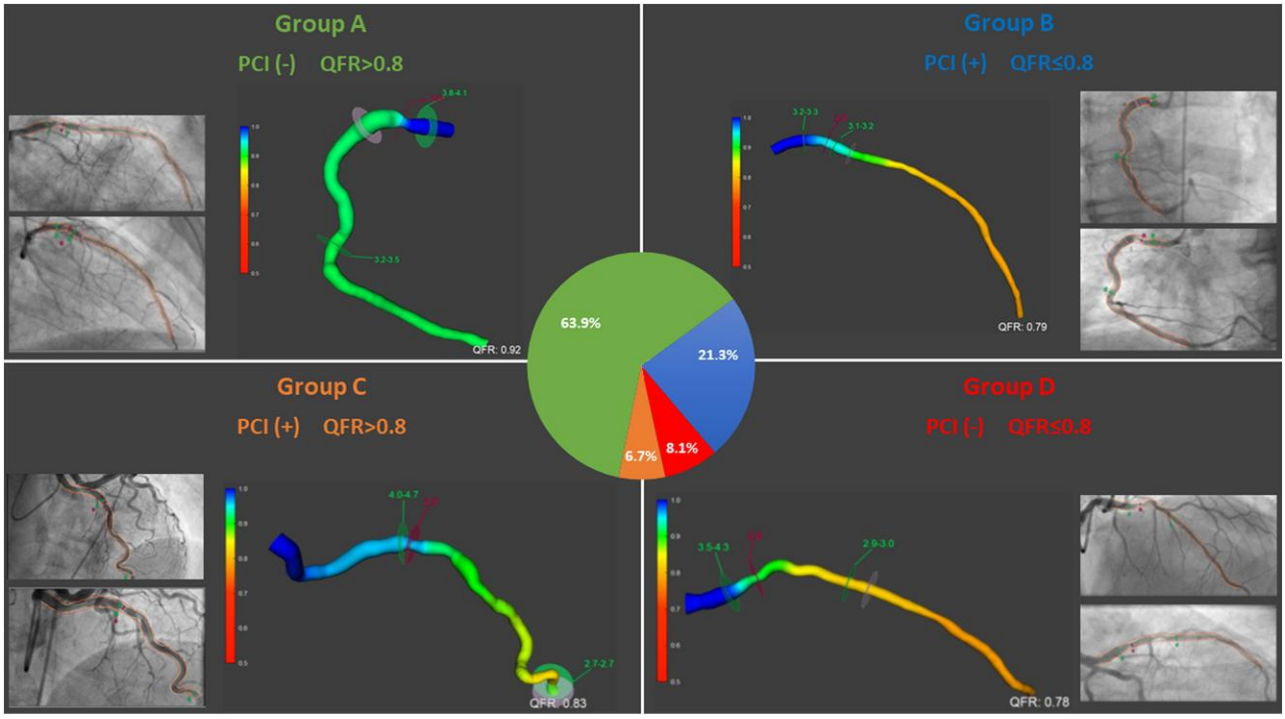


Figure 2 Presentation of vessel groups based on performing or deferring percutaneous coronary intervention and the quantitative flow ratio result with a cut-off point ≤0.8 indicating revascularization.

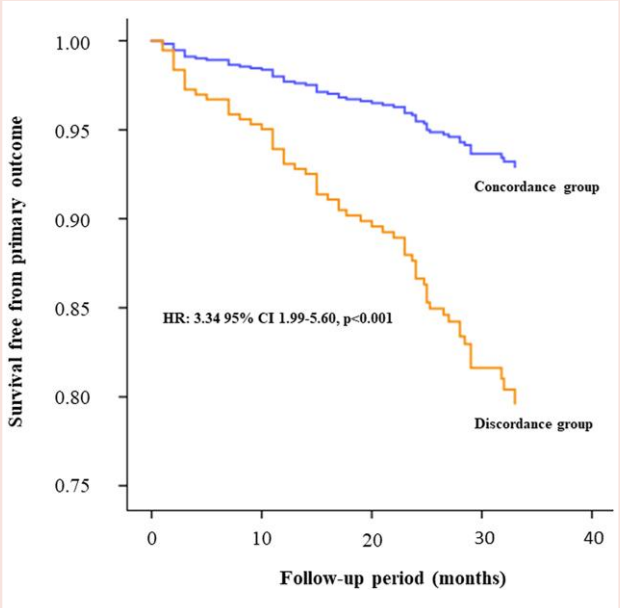


Figure 3 Survival free of the primary endpoint stratified by discordance between quantitative flow ratio and visual angiographic estimation. Patients in discordance group had a three-fold higher risk of presenting the composite outcome of cardiovascular death, myocardial infarction, and ischaemia-driven revascularization compared with concordance group after a median follow-up of 30.5 months.

Table 2 Hazard ratios for individual outcomes

	HR	Lower 95% CI	Upper 95% CI	*P*-value
Ischaemia-driven revascularization	3.69	1.80	7.30	<0.001
Cardiovascular death	3.52	1.43	7.59	0.001
Myocardial infarction	1.99	0.73	5.25	0.170
Composite outcome	3.34	1.99	5.60	<0.001

CI, confidence interval; HR, hazard ratio.

QFR results had a two-fold higher risk for MACEs during a 2-year follow-up period compared with patients with a revascularization plan consistent with QFR analysis. The authors also reported that higher risk was driven by undertreatment according to QFR, whereas cases where PCI was performed in disagreement with QFR were not associated with worse prognosis.[23] On the contrary, our results showed that despite deferring PCI in a functionally severe lesion (Group D) presented the highest risk for adverse cardiovascular events, performing PCI in a haemodynamically non-ischaemic vessel (Group C) was also related to a significant higher risk of VOCE in comparison with agreement groups. Of note, in the study by Zhang *et al.*,[23] all-cause mortality was part of the composite outcome instead of cardiovascular mortality as in our study and, in addition, the primary outcome of their study was inconsistent with the primary outcome of the randomized trial PANDA III from which the study population was originated. Moreover, the

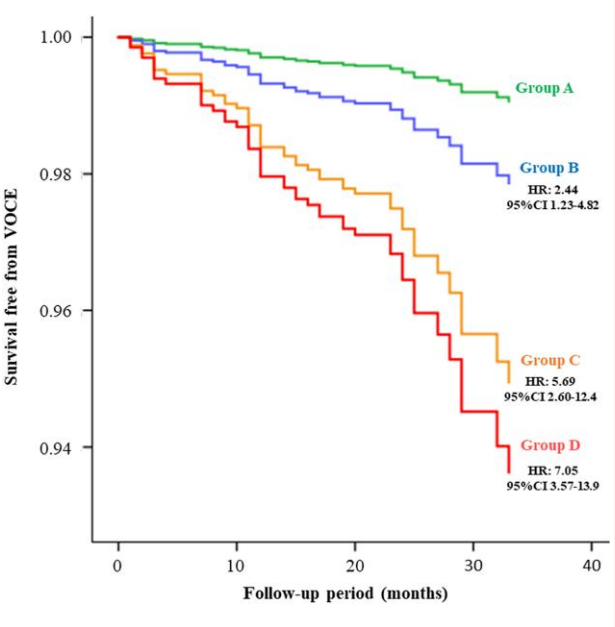


Figure 4 Survival free of vessel-oriented composite endpoint stratified by visual-functional agreement and disagreement vessel groups: Group A (PCI–, QFR > 0.8), Group B (PCI+, QFR ≤ 0.8), Group C (PCI+, QFR > 0.8) and Group D (PCI–, QFR ≤ 0.8). At vessel level, disagreement Groups C and D had a higher risk of presenting the composite outcome of vessel-related cardiovascular death, vessel-related myocardial infarction, and ischaemia-driven revascularization compared with agreement Groups A and B after a median follow-up of 30.5 months.

randomized FAVOR III China trial reported significant benefit in 1- and 2-year clinical outcomes of QFR- vs. angiography-guided revascularization.[11,12] In agreement with our findings, in FAVOR III China, the clinical benefit was greater among those patients in whom the pre-planned PCI strategy was changed by QFR, and the lower rate of adverse events in QFR group was driven by fewer events in both deferred and treated vessels.[11,12] In addition, a recent pooled analysis from the large trials FAVOR III China and PANDA III showed that PCI in vessels with QFR > 0.80 was associated with a three-fold increase of MI risk compared with medical treatment.[25] Accordingly, results from ISCHEMIA trial showed that an initial invasive strategy in stable coronary disease with documented moderate or severe ischaemia did not reduce cardiovascular events.[26] A novel finding of our study is that treating functionally non-ischaemic vessels with unnecessary procedures could increase cardiovascular risk, involving multiple cardiovascular outcomes.

Moreover, discordance between QFR and visual estimation in revascularization guidance was an adverse prognostic factor in patients presenting with either acute or chronic coronary syndrome. These findings are in line with the established value of functional assessment of lesions in chronic coronary syndrome[27] and, on the other hand, strengthen the recent evidence from both FFR and QFR trials that showed benefit from complete revascularization using physiology indices in the setting of acute coronary syndrome.[28–30]

The main strength of our study is the inclusion of all-comers representing a real-word cohort of patients undergoing coronary angiography, including high-risk patients that are often excluded in large trials. Nonetheless, several limitations should be noted. Firstly, the present study was of a retrospective design. Retrospective QFR analysis resulted in unsuccessful QFR computation in one-fourth of vessels. Thus, QFR calculation of all vessels was not feasible in all patients, meaning that a misclassification of patients in concordance and discordance groups cannot be ruled out. However, survival analysis was performed at both patient and vessel levels with similar results. Secondly, we included coronary vessels with minimal coronary artery disease (stenosis <30%) that have possibly led to overestimation of concordance between QFR and visual estimation in revascularization strategy, by disproportionately increasing the cases of deferring PCI in functionally normal vessels (Group A). However, our sample represents a real-life cohort reflecting everyday clinical practice. Lastly, patients in discordance group were older with more extended coronary artery disease compared with concordance group that could adversely affect their prognosis. However, after adjusting for these covariables, patients in discordance group had a significant higher risk of presenting the primary endpoint.

Conclusions

Discordance between QFR and visual estimation by plain coronary angiography in revascularization guidance was frequent and was found to be a strong predictor of worse prognosis after a median follow-up period of >2.5 years. Both deferring PCI in functionally significant lesions and performing PCI in functionally insignificant lesions increased the risk of adverse cardiovascular events.

Lead author biography

Dr Dimitrios Terentes-Printzios is an interventional cardiologist. He did research in interventional cardiology, hypertension, and cardiovascular disease prevention, recording more than 100 full-length publications with an H-index of 29. He concluded his PhD thesis on vascular ageing and was granted access to analyse large multicentre studies (SPRINT trial). He reviewed the recent ESH Guidelines on Hypertension in 2023, co-organized multicentre studies, performed meta-analyses that were included in the ESC Guidelines and is Executive Editor of the *Hellenic Journal of Cardiology*. He was a fellow in Interventional Cardiology in the John Radcliffe Hospital in Oxford and currently works in Hippokration Hospital.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Supplementary material

Supplementary material is available at *European Heart Journal Open* online.

Conflict of interest: None declared.

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