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Three-dimensional QCA-based vessel fractional flow reserve (vFFR) in Heart Team decision-making: a multicentre, retrospective, cohort study

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ABSTRACT

Objectives To evaluate the feasibility of three-vessel three-dimensional (3D) quantitative coronary angiography (QCA)-based fractional flow reserve (FFR) computation in patients discussed within the Heart Team in whom the treatment decision was based on angiography alone, and to evaluate the concordance between 3D QCA-based vessel FFR (vFFR)-confirmed functional lesion significance and revascularisation strategy as proposed by the Heart Team.

Design Retrospective, cohort.

Setting 3D QCA-based FFR indices have not yet been evaluated in the context of Heart Team decision-making; consecutive patients from six institutions were screened for eligibility and three-vessel vFFR was computed by blinded analysts.

Participants Consecutive patients with chronic coronary syndrome or unstable angina referred for Heart Team consultation. Exclusion criteria involved: presentation with acute myocardial infarction (MI), significant valve disease, left ventricle ejection fraction <30%, inadequate quality of angiogram precluding vFFR computation in all three epicardial coronary arteries (ie, absence of a minimum of two angiographic projections with views of at least 30° apart, substantial foreshortening/overlap of the vessel, poor contrast medium injection, ostial lesions, chronic total occlusions).

Primary and secondary outcome measures Discordance between vFFR-confirmed lesion significance and revascularisation was assessed as the primary outcome measure. Rates of major adverse cardiac events (MACE) defined as cardiac death, MI and clinically driven revascularisation were reported.

Results Of a total of 1003 patients were screened for eligibility, 416 patients (age 65.6±10.6, 71.2% male, 53% stable angina) were included. The most important reason for screening failure was insufficient quality of the angiogram (43%). Discordance between vFFR confirmed lesion significance and revascularisation was found in 124/416 patients (29.8%) corresponding to 149 vessels (46/149 vessels (30.9%) were reclassified as significant and 103/149 vessels (69.1%) as non-significant by vFFR). Over a median of 962 days, the cumulative incidence of MACE was 29.7% versus 18.5% in discordant versus concordant patients (p=0.031).

Conclusions vFFR computation is feasible in around 40% of the patients referred for Heart Team discussion, a limitation that is mostly based on insufficient quality of the angiogram. Three vessel vFFR screening indicated discordance between vFFR confirmed lesion significance and revascularisation in 29.8% of the patients.

Strengths and limitations of this study

- Multicentre, cohort study enrolling consecutive patients referred for coronary Heart Team consultation.
- Recently validated three-dimensional (3D) quantitative coronary angiography (QCA)-based vessel fractional flow reserve (vFFR) computed in all major epicardial coronary arteries.
- The present study is the first to evaluate a discordance between final revascularisation strategy based on routine angiographic screening and lesion significance as assessed by vFFR.
- Offline vFFR computation of the full coronary tree based on angiograms made in routine practice is feasible in around 40% of the patients referred for routine Heart Team discussion.
- Retrospective design and substantial drop out rate are noted limitations that need to be addressed in prospective studies with 3D-QCA advocated angiogram acquisition.

INTRODUCTION

The importance of a fractional flow reserve (FFR)-guided revascularisation strategy in patients with coronary artery disease (CAD) has been increasingly recognised.[1–3] As such, FFR-based invasive treatment deferral proved to be safe and superior to angiography-based decision-making.[1] In addition, among patients with multivessel disease (MVD) and intermediate coronary stenoses, invasive physiological assessment demonstrated to reclassify functional lesion significance in up to 45% of the cases.[4–8]

These findings are particularly relevant for guideline-recommended multidisciplinary Heart Team decision-making.[3 9]

Nevertheless, invasive functional lesion assessment carries inherent costs, time and patient discomfort in case an hyperemic agent is used and its penetration rate in clinical practice is still low.[3] Recently, three-dimensional (3D) quantitative coronary angiography (QCA)-derived FFR indices have been developed for less invasive functional lesion assessment and demonstrated a high linear correlation with invasively measured FFR and a high accuracy to detect lesions with FFR ≤0.80.[10–16] However, none of them have been evaluated in context of the Heart Team discussion to date.

Given this background, we aimed: (1) to evaluate the feasibility of performing three-vessel-vessel fractional flow reserve (vFFR) in patients discussed within the Heart Team in whom the treatment decision was based on angiography alone and (2) to evaluate the concordance between vFFR confirmed functional lesion significance and revascularisation strategy as proposed by the Heart Team.

METHODS

Study population and eligibility criteria

This is a retrospective, multicentre, cohort study enrolling patients referred for Heart Team consultation within the Erasmus Medical Center, Thorax Center, Rotterdam, The Netherlands. Consecutive patients with stable angina or unstable angina referred from six institutions in the Netherlands (Erasmus Medical Center, Sint Franciscus Gasthuis, Vlietland Hospital, Haven Hospital, IJsselland Hospital, Ikazia Hospital) between January 2015 and December 2017 were screened for eligibility. Referral for the coronary Heart Team consultation was at the discretion of each patient practitioner at the participating sites.

Exclusion criteria involved: FFR/iFR lesion severity evaluation prior to Heart Team consultation, presentation with acute myocardial infarction (MI), significant valve disease, left ventricle ejection fraction <30%, previous coronary artery bypass grafting (CABG), inadequate quality of angiogram precluding vFFR computation in all three epicardial coronary arteries (ie, absence of a minimum of two angiographic projections with views of at least 30° apart, substantial foreshortening or overlap of the vessel, poor contrast medium injection, ostial left or right CAD, tandem (serial) lesions in the vessel, chronic total occlusions) and unavailability of baseline aortic root blood pressure.

This retrospective study has been performed according to the Erasmus Medical Center regulations for the appropriate use of data in patient-oriented research, which are on the basis of international regulations, including the Declaration of Helsinki and its subsequent amendments. As it concerns database research with anonymous data, no Institutional Review Board or ethics committee approval is required.

Patient and public involvement

There was no patient or public involvement in the design or conduct of this research with anonymous data linking the anonymous data sets from six participating institutions.

vFFR analysis

Computation of vFFR was performed offline by three trained analysts (MT, KM, AV), blinded to patient data and Heart Team decision, using CAAS workstation V.8.1 (Pie Medical Imaging, Maastricht, The Netherlands).[11] Within CAAS Workstation, vFFR is computed based of pressure drop calculated by applying physical laws, including viscous resistance and separation loss effects present in coronary flow behaviour, as previously described.[11 17] Vessel geometry was derived from well-validated 3-D reconstructions reducing the effects of foreshortening, out-of-plane magnification and non-symmetric coronary lesions.[18 19]

vFFR analyses were performed in all three major epicardial arteries up to at least 2.25 mm of diameter, as assessed by QCA (online supplemental figure 1). A total of two 2-D angiographic views per each analysed vessel were exported and loaded into the software. Although temporal alignment of the cardiac cycle between the two angiograms was performed automatically by ECG triggering, manual frame selection was allowed. Contour detecting was performed semi-automatically. vFFR was calculated automatically incorporating the invasively measured aortic root pressure and automatically generated 3D QCA values and vFFR along the entire analysed vessel. The per cent diameter stenosis (%DS), minimal lumen diameter, reference lumen diameter and lesion length were also determined from the generated 3D vessel models. MVD was defined as a presence of >40% stenoses in ≥2 major epicardial vessels or left main CAD, as assessed by visual estimation by the Heart Team.[4]

vFFR-based lesion significance and treatment concordance

The vFFR-based functional lesion significance was compared against the treatment performed according to Heart Team recommendation. Discordance between vFFR confirmed lesion significance and revascularisation was evaluated using a vFFR threshold of ≤0.80, following the methodology of studies that evaluated FFR to guide treatment decisions.[2 7] In order to exclude vessels with lesions in segments with calibres below the threshold for revascularisation, vessels with diameters below 2 mm were not included in the reclassification analysis.[7] Likewise, vessels with diffuse disease, defined as diffuse wall irregularity without focal lesions (diameter stenosis 30%–70%), were not included in the reclassification analysis.

Discordance between vFFR confirmed lesion significance and revascularisation was defined as a difference between the vFFR confirmed number of vessels with functionally significant lesions and the number of vessels revascularised according to Heart Team recommendation. In case of 'jumping' grafts in patients undergoing

CABG, a vessel territory (right coronary artery (RCA), left anterior descending (LAD), CX) with at least one anastomosed vessel was considered as treated.

Discordance analyses were performed after unblinding vFFR results and patient data and was presented at patient (patients with at least one discordant vessel) and vessel level.

Clinical follow-up

Clinical follow-up data were obtained by reviewing electronic medical records of the hospital charts, outpatient clinical visits, telephone contact or by questionnaires sent by regular mail. Survival status was confirmed by automated civil registry checks. Major adverse cardiac events (MACE) were defined as a composite of cardiac death, MI, and ischaemia-driven (unplanned) revascularisation. All clinical outcomes were defined according to Academic Research Consortium definitions.[20] All deaths were considered cardiac unless an undisputable[21] non-cardiac cause was present.

Clinical events were compared in patients categorised according to presence of at least one vessel with discordance between vFFR-confirmed lesion significance and treatment.

Statistical analysis

Continuous variables were presented as mean±SD (normally distributed data) or median and IQR (non-normally distributed data) and compared using the Student's t-test or Wilcoxon rank sum tests. Categorical variables, showed as counts or percentages, were compared using the χ^2 or Fisher exact tests. The impact of vFFR on the vessel reclassification was evaluated by the Bowker-McNemar test.

Survival analysis was performed using the Kaplan-Meier method. Cox proportional hazards models, accounting for the multilevel nature of the data, were generated to evaluate the association between vFFR-confirmed lesion significance and treatment discordance and clinical outcomes. Adjustment variables included age, diabetes mellitus, impaired renal function, history of prior MI or percutaneous coronary intervention (PCI), left ventricular function and presence of MVD. In addition, as a sensitivity analysis, similar analyses were performed excluding patients treated conservatively (no PCI, no CABG) as there are potential variables such as frailty, poor vessel quality and other competing risks which may have lead the Heart Team to recommend no revascularisation in the conservative management group. All statistical analyses were performed using SPSS (V.25.0, SPSS). A p value of<0.05 was considered as statistically significant.

RESULTS

Between January 2015 and December 2017, there were 1603 coronary Heart Team consultations performed in 1049 patients; a total of 1003 patients, referred from one of the six centres participating in this study, were screened for eligibility (figure 1). Of them, 416 patients

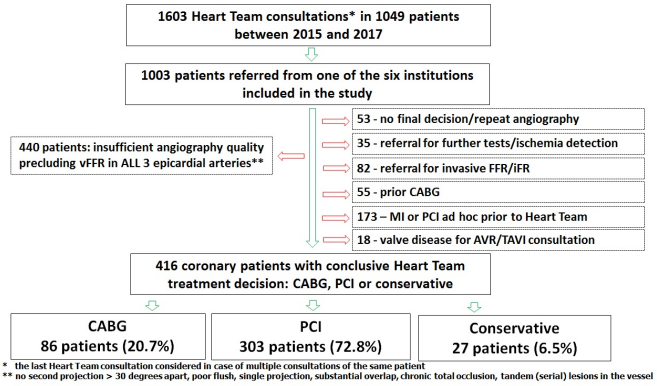

Figure 1 Flow chart of the study. In case of multiple consultations of the same patients, the final (last) Heart Team consultation was considered. Patients with fractional flow reserve (FFR)/iFR performed before Heart Team consultation and patients referred for FFR/iFR before reconsultation by the Heart Team were not included in the final concordance analysis between the vessel FFR (vFFR) confirmed lesion significance and revascularisation according to Heart Team recommendation. Patients referred primarily for severe valvular heart disease were discussed in a separate dedicated to valvular Heart Team. CABG, coronary artery bypass grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention, AVR - aortic valve replacement, TAVI - trancatheter aortic valve implantation

(mean age 65.6±10.6, 71.2% were men) were included in the concordance analysis. The most important reason for screening failure was insufficient quality of the coronary angiogram (43.9%; 440 patients) (figure 1). Baseline clinical and angiographic characteristics were not statistically different between patients included and not included in the final analysis.

Two hundred twenty patients (52.9%) presented with stable angina and 196 patients (47.1%) with unstable angina. Following Heart Team consensus, 86 patients (20.7%) underwent CABG, 303 patients (72.8%) underwent PCI and conservative treatment was advocated in 27 patients (6.5%). Diabetes mellitus, hypertension and dyslipidaemia were found in 35.6%, 67.5% and 52.6%, respectively (table 1).

A total of 159 patients (38.2%) underwent pre Heart Team ischaemia testing using cycle ergometry in 58 patients (36.5%) and non-invasive imaging tests in 126 patients (63.5%).

Overall, based on routine visual angiographic lesion assessment by the Heart Team, MVD was present in 334 patients (80.3%) (figure 2). Based on 3D-QCA analysis, MVD was identified in 288 patients (69.2%), whereas vFFR screening indicated the presence of functionally significant MVD in 214 (51.4%) patients (Bowker-McNemar test, p=0.001).

The mean 3D-QCA-based %DS was 45.67%±17.27%, median vFFR was 0.84 (0.69–0.93) (table 2, online supplemental figure 2).

Table 1 Baseline characteristics

	Overall (N=416)
Demographics	
Age (years), mean±SD	65.6±10.6
Male	296 (71.2%)
Hypertension	281 (67.5%)
Diabetes mellitus	148 (35.6%)
Dyslipidaemia	231 (55.5%)
Renal function impairment	30 (7.2%)
COPD	38 (9.1%)
Positive family history	127 (30.5%)
Smoking	66 (15.9%)
Previous PCI	105 (25.2%)
Previous MI	92 (22.1%)
Previous stroke or TIA	25 (6.0%)
Left ventricular function	
Normal	271 (65.1%)
Moderate	95 (22.8%)
Severe	50 (12.1%)
Clinical presentation	
Stable CAD	220 (52.9%)
Unstable angina	196 (47.1%)
Non-invasive diagnostics	
Overall*	159 (38.2%)
Stress ECG	58 (36.5%)
Stress echocardiography	5 (3.1%)
SPECT	46 (28.9%)
CT/MRI	75 (47.2%)

*in 25 patients more than one non-invasive diagnostic test was performed.
CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; SPECT, single-photon emission-CT; TIA, transient ischaemic attack.

vFFR assessment: coronary revascularisation concordance

Compared with coronary revascularisation as performed following Heart team recommendation, vFFR computation of each epicardial artery in the coronary tree indicated discordance between vFFR confirmed lesion significance and revascularisation in 124/416 patients (29.8%) corresponding to 149/1248 vessels (11.9%) (figure 3).

Of them, at least one discordant vessel was found in 26/86 (30.2%) patients treated with CABG, 88/303 (29.0%) patients treated with PCI and 10/27 (37.0%) managed conservatively.

Of the 149 discordant vessels, 46 vessels (30.9%) were reclassified as significant while the remaining 103 vessels (69.1%) were reclassified as non-significant by vFFR (online supplemental figure 3).

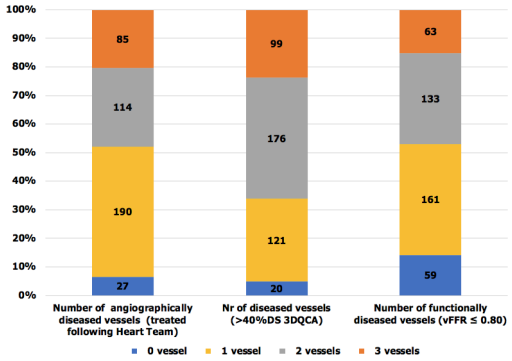

Figure 2 Angiographically diseased vessels (treated following Heart Team discussion), vessels diseased according to 3D-QCA (%DS >40%),[4] functionally diseased vessels (vFFR ≤0.80) (patient-level analysis). 3D-QCA, three-dimensional quantitative coronary angiography; %DS, percentage diameter stenosis; vFFR, vessel fractional flow reserve. Left main coronary artery analysed with left anterior descending artery as one vessel territory. *vFFR-based lesion significance versus revascularisation discordance in at least one vessel.

Discordance between vFFR confirmed lesion significance and revascularisation was found in 53/149 cases (35.6%) in left circumflex, in 52/149 cases (34.9%) in left anterior descending (LAD) and in 44/149 cases (29.5%) in right coronary artery (RCA).

Exploratory analyses of clinical outcomes in relation to vessel reclassification

Follow-up was available for 93% of patients. Over the median follow-up of 962 days (613–1299 days), the cumulative incidence of MACE was 29.7% versus 18.5% (adjusted HR 1.61, 95% CI 1.04 to 2.50, p=0.031) in patients with at least one vFFR-based lesion significance versus revascularisation discordance, compared with patients without any discordant vessels online supplemental table 1), after adjustment for age, diabetes mellitus, impaired renal function, history of prior MI or PCI, left ventricular function and presence of MVD. All-cause mortality rates were 14.4% versus 7.8% (adjusted HR 1.97, 95% CI 1.03 to 3.76, p=0.041) in the discordant versus the concordant group. Rates of MI and repeated revascularisation were 8.5% versus 4.1% (adjusted HR 2.30, 95% CI 0.97 to 5.42, p=0.058) and 14.5% versus 11.5% (adjusted HR 1.30, 95% CI 0.72 to 2.36, p=0.383) in patients with versus without any discordant vessel, respectively.

A sensitivity analysis performed in patients treated with either CABG or PCI (excluding conservatively managed group) brought consistent results. The cumulative incidence of MACE was 28.4% versus 18.4% (HR 1.59, 95% CI 1.01 to 2.52, p=0.046) in patients with at least one vFFR-based lesion significance versus revascularisation discordance, compared with patients without any discordant vessels. Rates of all-cause mortality, MI and repeated revascularisation were 11.9% versus 7.8% (adjusted HR 1.64, 95% CI 0.81 to 3.35, p=0.170), 9.3% versus 4.3% (adjusted HR 2.39, 95% CI 1.01 to 5.67, p=0.049) and

Table 2 Baseline angiographic characteristics (3D-QCA) and vFFR (vessel level)

	Overall vessels (N=1248)	RCA	LAD	CX
3D-QCA				
% DS. (mean±SD)	45.67±17.27	42.76±16.34	49.11±16.88	44.61±17.64
%DS >40% (n, %)	770 (61.7%)	226/770 (29.4%)	296/770 (38.4%)	248/770 (32.2%)
MLD (mean±SD)	1.69±1.57	1.87±0.78	1.50±0.57	1.74±0.74
RVD (mean±SD)	3.13±0.86	3.24±0.87	3.03±0.80	3.19±0.91
Lesion length (mm ±SD)	22.74±13.75	19.97±12.01	19.97±12.01	22.52±13.27
Proximal segment diseased (n, %)	587/770 (76.2%)	142/226 (62.8)	269/296 (90.9%)	176/248 (71.0%)
vFFR				
vFFR (IQR)	0.84 (0.69–0.93)	0.88 (0.75–0.96)	0.77 (0.65–0.86)	0.89 (0.73–0.97)

CX, left circumflex artery; D-QCA, three-dimensional quantitative coronary angiography; %DS, percentage diameter stenosis; LAD, left anterior descending artery; MLD, minimum lumen diameter; RCA, right coronary artery; RVD, reference vessel diameter; vFFR, vessel fractional flow reserve.

15.7% versus 11.4% (adjusted HR 1.44, 95% CI 0.79 to 2.64, p=0.235) in patients with versus without any discordant vessel, respectively.

Further analyses stratified according to type of vFFR-based lesion significance versus revascularisation discordance indicated that the presence of a discordant vessel reclassified as significant (not revascularised, significant by vFFR) was associated with a higher risk of MACE (adjusted HR 2.77, 95% CI 1.52 to 5.06, p=0.001) and all-cause mortality (adjusted HR 4.25, 95% CI 1.84 to 9.85, p=0.001), but not with a higher risk of MI (adjusted HR 0.26, 95% CI 0.04 to 1.80, p=0.171) or repeated revascularisation (adjusted HR 1.51, 95% CI 0.59 to 3.89, p=0.395). Presence of a discordant vessel resclassified as non-significant (revascularised, non-significant by vFFR) was not associated with a higher risk of MACE (adjusted HR 1.04, 95% CI 0.64 to 1.69, p=0.868) or other outcome variables.

There were no statistically significant differences in the rates of MACE (22.2% vs 18.5%, adjusted HR 1.31, 95% CI 0.85 to 2.01, p=0.226) or other outcome variables in patients with angiographically confirmed MVD versus patients without MVD. In patients with vFFR-confirmed MVD, there was a trend towards higher rates of MACE (25.0% vs 17.9%, adjusted HR 1.47 95% CI 0.96 to 2.26, p=0.078) and MI (8.1% vs 3.7%, HR 2.14 95% CI 0.84 to 5.41, p=0.109), although the numerical differences did not reach a statistically significant level.

DISCUSSION

The present study is the first to assess the feasibility of three-vessel 3D-QCA based vFFR screening in patients undergoing routine Heart Team discussion. Offline vFFR computation of the full coronary tree based on angiograms made in routine practice is feasible in around 40% of the patients referred for routine Heart Team discussion, a limitation that is mostly based on insufficient quality of the referred angiograms. Nevertheless, in patients amenable for 3-vessel vFFR analyses, we observed a discordance between final revascularisation strategy based on routine angiographic screening and lesion significance as assessed by vFFR in at least one vessel in 29.8% of patients. Exploratory analyses of long-term clinical events indicated higher mortality and MACE rates in patients in whom discordance was found, a finding that is in line with previous studies showing that in case the information derived from invasive FFR was disregarded, a poorer outcome was observed.[22]

With reported numbers on inappropriate use of CABG and PCI in about 2%–15% of the cases, respectively, recent guidelines on myocardial revascularisation called for optimisation of treatment decisions using multidisciplinary and multimodality diagnostics-based Heart Team decision process.[9 23 24] As such, integrated physiological lesion assessment has been recently recognised to improve decision-making for patients undergoing either PCI and CABG.[1 25 26] Following earlier data on stenting non-functionally significant lesions, also grafting of functionally insignificant lesions has been associated with an increased risk of periprocedural events, early graft failure and acceleration of native coronary atherosclerosis.[27 28]

One of the first studies assessing the impact of FFR on revascularisation strategy was performed by van Belle *et al* who concluded that the use of FFR in approximately 1.7 vessels per patient resulted in a change in revascularisation strategy in about half of the cases, a number that appeared to correlate to the number of vessels assessed by FFR[4 5] (online supplemental table 2). The ongoing RIPCORD 2 trial is currently assessing the feasibility of complete 3-vessel FFR screening.[29]

However, given known issues with multivessel invasive functional lesion assessment as pressure wire durability, drift, time, contrast use and optionally multiple episodes of hyperaemia, the use of 3D-QCA based technologies might offer substantial benefits in time, costs and patient

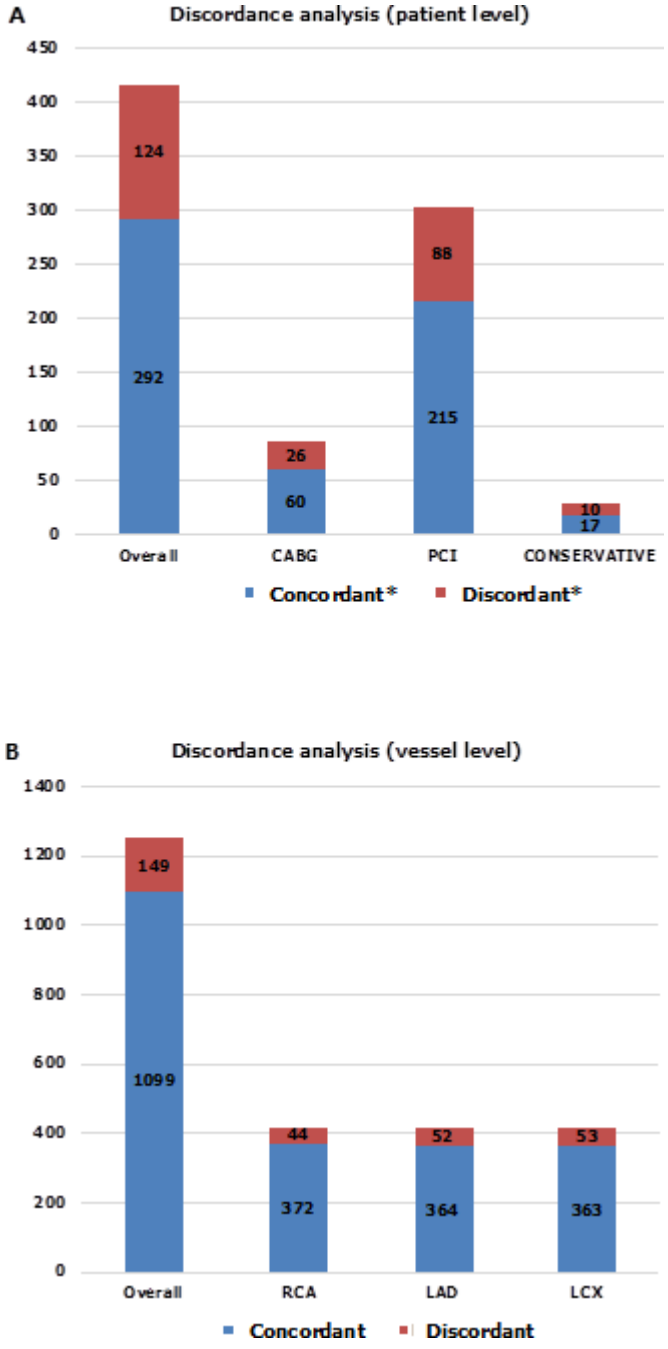

Figure 3 Discordance between the vFFR confirmed lesion significance and revascularisation according to Heart Team recommendation at the patient level and vessel level. 3D-QCA, three-dimensional quantitative coronary angiography; %DS, percentage diameter stenosis; vFFR, vessel fractional flow reserve. Left main coronary artery analysed with left anterior descending artery as one vessel territory. *vFFR-based lesion significance versus revascularisation discordance in at least one vessel.

burden and open the door to a more widespread adoption of functional lesion assessment in routine practice.

In the present study, excluding patients with FFR prior to the Heart Team discussion, the use of 3D-QCA based vFFR resulted in the reclassification of a considerable number of patients (29.8%) in which incorporation of functional information from vFFR could have significantly changed the treatment recommendation.

Our findings underline the importance of a complete physiological assessment prior to Heart Team decision-making and the use of vFFR could confer an opportunity for those performing diagnostic cardiac catheterisation only without access to pressure wires or microcatheters. The latter could substantially optimise referral patterns and improve Heart Team decision-making.[30] Furthermore, a low variability in the vFFR assessment as performed by a blinded core lab or by independent local personnel in the individual participating centres has been proven in the recent FAST II (NCT03791320) study indicating the reliability of physiological lesion assessment using vFFR by trained local site personnel in the absence of a well-trained core lab.[31] However, the number of cases discussed within our Heart Team not amenable for 3-vessel vFFR computation due to insufficient quality of the angiogram was 43% suggesting that an improvement in routine diagnostic coronary angiograms is needed. Particular attention should be paid to optimal projections (>30° apart), minimised overlap and brisk contrast injection.

The exclusion rate in this study should be also considered in light of the specific exclusion criteria such as chronic total occlusions, which also preclude three-vessel vFFR screening of the angiogram.

Our hypothesis-generating analysis calls for a prospective, randomised study allowing to assess the potential causality between 3-vessel-vFFR screening as part of Heart Team discussion, final treatment recommendation and clinical safety and efficacy of such an approach.

The use of non-invasive diagnostics for ischaemia detection in this cohort, including single-photon emission-computed tomography (SPECT), was similar to previous reclassification studies that evaluated reclassification of treatment strategy based on invasive FFR.[4] As such, in the present study, only 46 patients (11.1%) underwent a preprocedural diagnostic test that could have shown localisable ischaemia.

Limitations

The study has to be viewed in the light of the following limitations. Although consecutive patients were clinically and angiographically screened for eligibility, some selection bias cannot be excluded. In prior invasive FFR-based reclassification studies, investigators were asked to *prospectively* define their management strategy based on angiography alone and second including the invasively measured FFR values.[4] In the present retrospective study, we refrained from attempts to evaluate final recommendation reclassification (CABG vs PCI vs conservative management) given a number of unmeasurable or unidentifiable confounders that could bias such analysis, such as frailty or technical consideration related to CABG/PCI. Finally, vFFR was assessed offline by trained analyst, however without an independent core lab, and angiograms made in routine practice were used, obtained without specific image acquisition guidelines which currently exist for

3D-QCA based FFR technologies.[11 13] Nevertheless, the FAST II study has recently demonstrated a good correlation between dedicated core lab vFFR and pressure wire-based FFR (R=0.74; p<0.001; mean bias 0.0029±0.0642) and an excellent diagnostic accuracy of vFFR in identifying lesions with an invasive wire-based FFR ≤0.80 (AUC 0.93; 95% CI 0.90 to 0.96; p<0.001) also in more complex lesions, including bifurcations, tortuous and calcified lesions (NCT03791320).[31] The safety of treatment planning solely based on angiography-derived functional indices still remains to be confirmed in currently ongoing, clinical outcome studies (NCT03729739, NCT04931771). In light of the scope of the present study, vFFR calculations were performed offline by trained operators, as such, we refrained from reporting vFFR computation times. Differences in time to computate online vFFR (typically 1–2 min) and time to perform routine invasive FFR assessment will be reported in the recently initiated randomised FAST III trial (NCT04931771).

CONCLUSIONS

The 3D-QCA based vFFR in all three epicardial coronary arteries is feasible in around 40% of the patients referred for routine Heart Team discussion, a limitation that is mostly based on insufficient angiography quality. Furthermore, three vessel vFFR screening indicated discordance between vFFR confirmed lesion significance and revascularisation in 29.8% of the patients referred to the Heart Team.

Contributors All authors contributed to the interpretation of the results and writing of the manuscript. MT and JD prepared the study design. MT and JD wrote the first version of the manuscript. MT, KM, TN, ITK, AV, LJCvZ, NVB, BMvD, LKS, IK and JD collected and analysed the data. MT, WKdD, IK, JMW, RD, FZ, NMVM and JD revised the manuscript, the data analysis and contributed to the revision of the manuscript. MT and JD accept full responsibility for the work and the conduct of the study, had access to the data, and controlled the decision to publish.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This retrospective study has been performed according to the Erasmus Medical Center regulations for the appropriate use of data in patient-oriented research, which are on the basis of international regulations, including the Declaration of Helsinki and its subsequent amendments. As it concerns database research with anonymous data, no Institutional Review Board or ethics committee approval is required.

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Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. All data relevant to the study are included in the article or uploaded as supplementary information. Should further details or materials be required, please contact the authors.

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