EuroIntervention
2024;20:561-570
DOI: 10.4244/EIJ-D-23-00674

ORIGINAL RESEARCH

Quantitative flow ratio versus fractional flow reserve for Heart Team decision-making in multivessel disease: the randomised, multicentre DECISION QFR trial

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This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-23-00674

ABSTRACT

BACKGROUND: Vessel-level physiological data derived from pressure wire measurements are one of the important determinant factors in the optimal revascularisation strategy for patients with multivessel disease (MVD). However, these may result in complications and a prolonged procedure time.

AIMS: The feasibility of using the quantitative flow ratio (QFR), an angiography-derived fractional flow reserve (FFR), in Heart Team discussions to determine the optimal revascularisation strategy for patients with MVD was investigated.

METHODS: Two Heart Teams were randomly assigned either QFR- or FFR-based data of the included patients. They then discussed the optimal revascularisation mode (percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG]) for each patient and made treatment recommendations. The primary endpoint of the trial was the level of agreement between the treatment recommendations of both teams as assessed using Cohen's kappa.

RESULTS: The trial included 248 patients with MVD from 10 study sites. Cohen's kappa in the recommended revascularisation modes between the QFR and FFR approaches was 0.73 [95% confidence interval {CI}: 0.62-0.83]. As for the revascularisation planning, agreements in the target vessels for PCI and CABG were substantial for both revascularisation modes (Cohen's kappa=0.72 [95% CI: 0.66-0.78] and 0.72 [95% CI: 0.66-0.78], respectively). The team assigned to the QFR approach provided consistent recommended revascularisation modes even after being made aware of the FFR data (Cohen's kappa=0.95 [95% CI:0.90-1.00]).

CONCLUSIONS: QFR provided feasible physiological data in Heart Team discussions to determine the optimal revascularisation strategy for MVD. The QFR and FFR approaches agreed substantially in terms of treatment recommendations.

SUBMITTED ON 12/08/2023 - REVISION RECEIVED ON 1st 25/01/2024/ 2nd 23/02/2024 - ACCEPTED ON 23/02/2024

Personalised medicine emphasises the importance of treatment decision-making based on individual risks[1]. In patients with multivessel disease (MVD) requiring revascularisation, an appropriate revascularisation mode (percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG]) should be considered. Multidisciplinary Heart Teams are essential for determining the optimal treatment strategy. In Heart Team discussions, the SYNTAX score (SS) is a crucial decision aid, as it is a risk assessment tool dedicated to patients with MVD that considers individual coronary anatomy[2]. The latest iteration of the SS (SYNTAX score II 2020 [SSII]) considers the patient's clinical characteristics, such as age and comorbidities, in addition to coronary anatomy, and provides 5- and 10-year prognostic estimates for each revascularisation mode[3]. These estimates can be fundamental for decision-making during Heart Team discussions.

The functional SYNTAX score (FSS), which scores only physiologically significant lesions, is another approach for improving the prognostic accuracy of the SS. The FSS, based on wire-derived fractional flow reserve (FFR), reportedly yielded better risk stratification than the anatomical SS scoring lesions with a visually estimated diameter stenosis of ≥50%[4]. However, implementing the FFR-based FSS may pose practical challenges, because multivessel interrogations of FFR induce the potential risk of wire-related complications and excess procedure time. Recently, angiography-derived FFR, an FFR simulation derived from angiography, has emerged with the outstanding advantages of not requiring a pressure wire or pharmacological hyperaemia[5,6]. With these advantages, angiography-derived FFR can potentially address wire-related issues in FSS calculations. The quantitative flow ratio (QFR) (Medis Medical Imaging Systems) is the first European Conformity (CE)- marked angiography-derived FFR whose diagnostic performance has been well confirmed[7]. In a *post hoc* analysis of the SYNTAX II trial, the FSS based on QFR (FSS_{QFR}) demonstrated better prognostic capability than the anatomical SS for predicting 2-year patient-oriented cardiovascular events[8]. However, the feasibility of using QFR as physiological data for Heart Team decision-making has not been investigated. The current trial aimed to evaluate the feasibility of using QFR, including the FSS_{QFR} and FSS_{QFR}-based SSII ($SSII_{QFR}$), in Heart Team discussions to decide on the treatment of patients with MVD.

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Impact on daily practice

The accurate prognostic assessment of patients with multivessel disease (MVD) following revascularisation can significantly inform the decisions of Heart Teams regarding the optimal revascularisation strategy. The quantitative flow ratio (QFR), as well as the fractional flow reserve (FFR), has also been recognised for augmenting the prognostic precision of the SYNTAX score (SS). However, the feasibility of using QFR during the Heart Team discussion remains to be thoroughly evaluated. The findings of this trial underscore the viability of QFR as a favourable alternative to wire-based FFR within Heart Team discussions for MVD patients. Utilising QFR eliminates the need for invasive FFR measurement procedures across multiple vessels and reduces procedural time, thereby enhancing the overall practicality of the functional SS, which conventionally requires physiological assessment using a pressure wire.

Methods

STUDY DESIGN

The DECISION QFR (The DEtermination of the appropriate proCedure of revascularization In the multidisciplinary Heart Team discusSION based on Quantitative Flow Ratio) trial was a prospective, multicentre, randomised controlled trial that aimed to investigate the feasibility of using QFR-based physiological data in decision-making for optimal treatment during Heart Team discussions. The trial included patients with MVD who required revascularisation (PCI or CABG). The detailed rationale and design of this trial have been previously published[9]. In the trial, two Heart Teams were randomly assigned to the patient data based on either the QFR (QFR approach) or FFR (FFR approach). Our primary hypothesis was that there would be a high level of agreement in treatment recommendations made based on QFR or FFR data **(Figure 1)**. All patients were assessed by both Heart Teams.

Each Heart Team examined the patient data, including blinded physiological data. QFR data for each patient included QFR values in each vessel, FSS_{QFR} and $SSII_{QFR}$. The FFR data for each patient included the FFR values in each vessel, FSS_{FFR} and $SSII_{FFR}$. Heart Team members were randomly assigned to either the QFR or FFR approach using an adaptive randomisation approach in a web-based randomisation module. The research ethics committee of each participating institution approved the study protocol. All enrolled patients provided written informed consent. This trial was registered with the University Hospital Medical Information Network (UMIN000040475).

INCLUSION AND EXCLUSION CRITERIA

The inclusion and exclusion criteria for the current trial are listed in **Supplementary Appendix 1**. Briefly, the trial enrolled patients with chronic coronary syndrome who had MVD involving proximal left anterior descending artery (LAD) lesions and required revascularisation (PCI or CABG). We excluded patients with specific anatomical conditions or comorbidities unsuitable for QFR analysis (i.e., aorto-ostial

Abbreviations

ARD	absolute risk difference	**FSS**	functional SYNTAX score	**PCI**	percutaneous coronary intervention
AUC	area under the curve	**ICC**	interclass correlation coefficient	**QFR**	quantitative flow ratio
CABG	coronary artery bypass grafting	**IQR**	interquartile range	**SS**	SYNTAX score
FFR	fractional flow reserve	**MVD**	multivessel disease	**SSII**	SYNTAX score II 2020

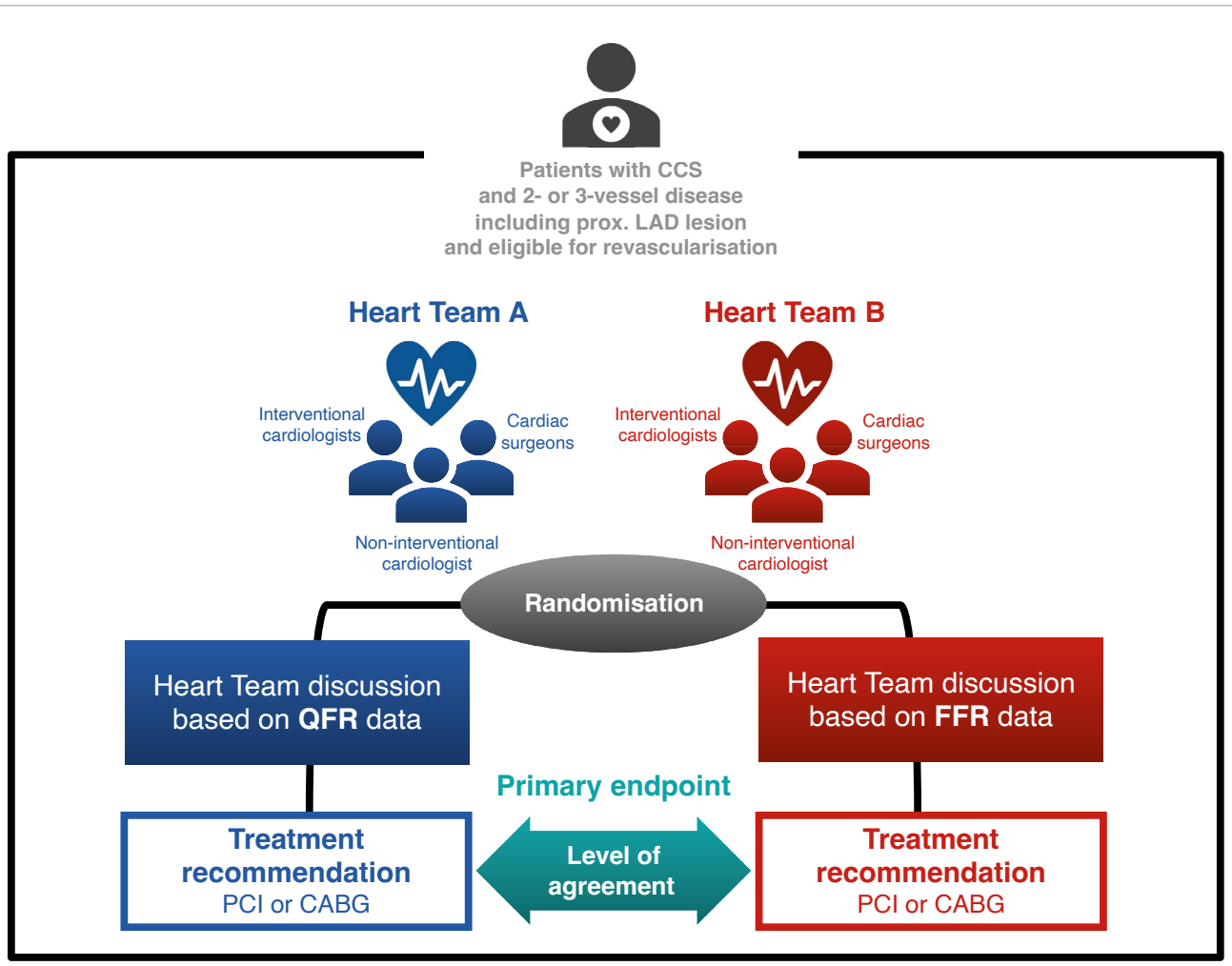


Figure 1. *Trial design of the DECISION QFR study. The DECISION QFR trial is a multicentre randomised controlled trial investigating the feasibility of using QFR-based patient data to determine the optimal revascularisation strategy in Heart Team discussions. We assessed the agreement between the treatment recommendations based on QFR and those based on FFR. The primary endpoint was agreement between the recommended treatment options based on QFR and FFR approaches, as assessed using Cohen's kappa. CABG: coronary artery bypass grafting; CCS: chronic coronary syndrome; FFR: fractional flow reserve; LAD: left anterior descending artery; PCI: percutaneous coronary intervention; QFR: quantitative flow ratio*

lesion, left main disease, advanced chronic kidney disease, atrial fibrillation, and patients who had previously undergone CABG) at the time of angiography. The trial recruited patients from 10 Japanese sites, as listed in **Supplementary Appendix 2**.

CORONARY ANGIOGRAPHY AND FFR ANALYSIS

To ensure sufficient imaging quality for QFR analysis, the investigators were encouraged to perform invasive coronary angiography in at least two projections on lesions that required clear visualisation without vessel shortening or overlapping. Use of the prespecified protocol was also recommended, including the use of specific projection angles which are listed in **Supplementary Appendix 3**.

Lesions with intermediate stenosis (visually estimated diameter stenosis of 50-90%) were investigated using a pressure wire to acquire FFR values. FFR values were measured at the distal part of the target lesions, and a pressure sensor was positioned at the part of the vessel with a diameter of ≥2.0 mm. The procedure time for FFR measurement (from zeroing the pressure wire to finishing all interrogations for all lesions) was recorded.

QFR ANALYSIS

We analysed the QFR in each vessel in which FFR was investigated. Experienced analysts performed offline QFR analysis using QAngio XA 3D version 2.0 (Medis Medical Imaging Systems) at an independent core laboratory (St. Luke's International Hospital, Tokyo, Japan). The analysts were blinded to the FFR values. Details of the QFR calculations have been reported elsewhere[10]. The QFR was analysed in the segment between the ostium of the main vessels (i.e., LAD, right coronary artery, and left circumflex artery) and the anatomical site where FFR was interrogated. The procedure time for QFR analysis (from opening the cine files on the software to finishing the analyses for all lesions) was recorded.

CALCULATION OF THE SYNTAX SCORE, SYNTAX SCORE II 2020, AND FUNCTIONAL SYNTAX SCORE

The SS and FSS values were calculated at the core laboratory using a web calculator (https://www.syntaxscore.org). To calculate FSS_{FFR} and FSS_{QFR}, we summed the individual scores of lesions only in physiologically significant vessels (i.e., QFR or FFR ≤0.8) and excluded physiologically non-significant vessels[7]. To quantify patient risk considering coronary anatomy and patient characteristics, we calculated the SSII. The SSII yields two predicted risks: 5-year major adverse cardiovascular event and 10-year mortality for PCI and CABG[3]. Because the Heart Teams discussed the optimal treatment recommendations based on anatomical and physiological data, SSIIs were also calculated based on the FSS in addition to the anatomical SS. Thus, the $SSII_{FFR}$ and $SSII_{QFR}$ were generated using the FSS_{FFR} and FSS_{QFR}, respectively. The Heart Teams referred to the predicted absolute risk difference (ARD) between PCI and CABG, which represents an absolute excess risk after PCI treatment compared with CABG treatment (i.e., predicted risk after PCI treatment [%] – predicted risk after CABG treatment [%]), for determining their treatment recommendation. A positive ARD means that PCI has an excessive mortality risk as compared with CABG, numerically suggesting a beneficial prognostic effect of CABG.

DECISION-MAKING ON TREATMENT RECOMMENDATIONS BY THE HEART TEAMS

The two centralised Heart Teams comprised three cardiologists (two interventional cardiologists and one non-interventional cardiologist) and two cardiac surgeons at St. Luke's International Hospital. The hospital conducts daily Heart Team discussions with experienced cardiologists and surgeons to determine optimal treatments for various heart conditions. The establishment of two central Heart Teams from the experienced institution ensures consistent, objective, and high-quality decision-making, thus minimising individual biases. Prior to this trial, a pretest showed substantial agreement (Cohen's kappa=0.63 [95% confidence interval {CI}: 0.25-1.00]) between these teams in treatment recommendations for 21 patients, using identical patient information[9]. These teams virtually discussed treatment strategies for patients enrolled from 10 participating sites. Virtual Heart Team discussions were held for each patient to decide on the optimal revascularisation strategy (PCI or CABG) by referring to the allocated physiological data and other basic patient data (i.e., patient background, cineangiography, and anatomical SS). The optimal treatment recommendation was selected from the following options: "CABG only", "equipoise", and "PCI only". Details are provided in **Supplementary Appendix 4**.

Based on the allocated physiological data, the Heart Teams discussed the indications for revascularisation for each vessel with anatomical stenosis.

The Heart Teams made two treatment decisions: the first was made with blinded allocation and the second after allocation unblinding. After the first decision, each team was provided allocation data and opposite functional data (FFR data for the QFR approach and QFR data for the FFR approach), and the second decision was made after the data were equally distributed to both teams (unblinded decision).

ENDPOINTS

The primary endpoint of the current trial was the level of agreement in treatment recommendations between the QFR and FFR approaches. The level of agreement was assessed with Cohen's kappa calculated based on two decision components: "CABG only" and "equipoise/PCI only". To apply this method, we referred to a previous study that investigated the level of agreement between two Heart Teams regarding their decision on revascularisation strategy for patients with MVD[11]. We treated "CABG only" as a distinct category due to its exceptional nature, considering the potential increase in mortality if a patient suitable only for CABG (such as in cases of significant ARD) were to receive PCI[12,13]. The secondary endpoints were as follows: (1) the availability rate of the FSS_{QFR}, owing to a full set of analysable QFR in a coronary tree; (2) the level of agreement in target vessels between the QFR and FFR approaches for revascularisation; (3) the level of agreement between the decision based on QFR data (blinded decision) and the decision made after knowing the FFR data (unblinded decision) within the QFR approach; (4) the level of agreement between the FSS_{QFR} and FSS_{FFR}, assessed with the interclass correlation coefficient (ICC); (5) the procedure time of QFR analyses compared with that of FFR measurements; and (6) the incidence rate of complications during FFR measurements.

STATISTICAL CONSIDERATIONS AND SAMPLE SIZE CALCULATION

For the primary endpoint, a kappa value of 0.61-0.80 between the two ratings was interpreted as "substantial agreement", and a kappa value of 0.41-0.60 was considered "moderate agreement"[14]. The level of decision agreement was expected to be substantial (kappa >0.60), and the trial would be considered successful if the lower boundary of the 95% CI was >0.40. We assumed that both teams would recommend "CABG only" in 20% of the enrolled patients with a kappa of 0.60. The detailed rationale of the assumptions in this trial has been described elsewhere[9]. Based on these assumptions, a sample size of 235 was sufficient to achieve 80% power and a positive trial with a 2-sided alpha of 0.05. Assuming an attrition rate of 10% to account for non-analysable cases, 260 patients were included.

Data are expressed as mean±standard deviation or median with interquartile range (IQR). Categorical variables were compared using Pearson's chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared using t-tests. Unless otherwise specified, a 2-sided p-value of <0.05 was considered statistically significant.

The difference in procedural time between QFR and FFR was assessed using the Wilcoxon signed-rank test. The level of correlation and agreement between QFR and FFR were determined using Pearson's correlation coefficient, Passing-Bablok regression analysis, and the Bland-Altman method. The agreement between the FSS_{QFR} and FSS_{FFR} was assessed using ICC. The discrimination ability of QFR for predicting an FFR of ≤0.80 was quantified using the receiver operating characteristic curve, and the areas under the curve (AUCs) were compared between analyses with and without the pre-specified angiographic protocol using the DeLong method[15]. All statistical analyses were performed using R software, version 4.2.2 (R Foundation for Statistical Computing).

Results

Between August 2020 and October 2021, among 527 screened patients, 260 patients were enrolled. The patient flowchart and reasons for excluding patients in the eligibility assessment are presented in **Supplementary Appendix 5** and **Supplementary Appendix 6**, respectively. In the 260 enrolled patients, coronary angiography detected 983 lesions with ≥50% stenosis. In these patients, a total of 507 vessels with intermediate stenosis (50-90%) were investigated using FFR **(Supplementary Appendix 7)**. Four patients (1.5% [4/260]) experienced complications during FFR measurement. Of those, one had hypotension, one had arrhythmia, and two had vessel injury induced by the pressure wire. In 507 vessels with FFR measurements, 11 vessels could not be analysed for QFR (vessel-level analysability rate of QFR: 97.8% [496/507]). Thus, four patients were excluded because they did not have a full set of analysable QFR in a coronary tree for FSS calculation (availability rate of the FSS_{QFR}: 98.5%). In total, 12 patients were excluded for reasons described in **Supplementary Appendix 5**, and 248 patients with 483 FFR and QFR measurements were included in the primary analysis. Patient characteristics are presented in **Table 1**. The mean number of lesions with visually estimated diameter stenosis ≥50% was 3.9±1.4. The prevalence of three-vessel disease was 58.1% and the mean anatomical SS was 20.9±9.3 points.

FFR MEASUREMENT AND QFR ANALYSIS

A total of 483 vessels in 248 patients were investigated using FFR and subsequently analysed for QFR. The median QFR and FFR were 0.77 (IQR: 0.67-0.87) and 0.76 (IQR: 0.69-0.85), respectively. The procedure time of QFR analysis per vessel was significantly shorter than that of FFR measurement (7.97 min [IQR: 6.30-10.08] vs 8.38 min [IQR: 6.00-13.23]; p=0.035) **(Supplementary Appendix 8)**. In patients who underwent angiography according to the prespecified protocol (n=76, 30.6%), the difference was further pronounced (6.65 min [IQR: 5.47-8.18] vs 10.17 min [IQR: 7.03-13.59]; p< 0.001). However, when categorising the groups according to the two methods of hyperaemic administration (contentious intravenous [CIV] or intracoronary [IC] administrations), the QFR procedure time was significantly shorter than the FFR procedure time in cases with CIV administration, whereas this difference disappeared in cases with IC administration **(Supplementary Appendix 9)**.

In the 483 vessels, the correlation coefficient between QFR and FFR was 0.68 [95% CI: 0.63-0.73] **(Supplementary Appendix 10)**. The AUC of QFR for predicting FFR ≤0.80 was 0.88 [95% CI: 0.84-0.91], whereas the sensitivity, specificity, positive predictive value, and negative predictive value of QFR were 0.83 [95% CI: 0.78-0.87], 0.82 [95% CI: 0.75-0.88], 0.90 [95% CI: 0.86-0.93], and 0.72 [95% CI: 0.65-0.78], respectively. The AUC in patients undergoing angiography following the prespecified protocol had a diagnostic performance comparable to that of patients for whom the protocol was not followed (AUC: 0.89 vs 0.86; p=0.367).

Physiological data and SSs are summarised in **Supplementary Appendix 11**. In the 248 patients, the median FSS_{QFR} and FSS_{FFR} were 18.01±9.74 and 18.59±9.96, respectively. The ICC between the FSS_{FFR} and FSS_{QFR} was 0.94 [95% CI: 0.93-0.95] **(Figure 2A)**. The mean predicted 10-year mortality risks after PCI derived from the $SSII_{QFR}$ and $SSII_{FFR}$ were 35.0±20.8% and 35.2±20.9%, respectively. The ICC for the ARD in 10-year mortality between the $SSII_{FFR}$ and $SSII_{QFR}$ were 0.97 [95% CI: 0.96-0.97] **(Figure 2B)**.

Table 1. Patient and anatomical characteristics.

Patient characteristics	N=248
Age, years	70.8±10.2
Male	195 (78.6)
Body weight, kg	65.2±13.1
BMI, kg/m^2	24.5±3.8
Hypertension	201 (81)
Diabetes mellitus	120 (48.4)
Diabetes with insulin treatment	15 (6)
Dyslipidaemia	193 (77.8)
Current smoker	57 (23)
History of myocardial infarction	30 (12.1)
History of aortic disease	11 (4.4)
History of PAD	16 (6.5)
History of stroke	16 (6.5)
COPD	7 (2.8)
LVEF, %	59.3±11.8
Haemoglobin, g/dL	13.8±1.8
Creatinine, mg/dL	0.9±0.5
Anatomical characteristics	
Number of lesions with ≥50% stenosis	3.9±1.4
3-vessel disease	144 (58.1)
Diseased vessel	
RCA	197 (79.4)
LAD	248 (100)
LCx	194 (78.2)
Anatomical SYNTAX score	20.9±9.3
SYNTAX score II 2020 based on angiographic stenosis	
5-year MACE estimate after PCI, %	25.4±14.1
5-year MACE estimate after CABG, %	19±10.4
ARD in 5-year MACE estimates, %*	6.3±5.1
10-year mortality estimate after PCI, %	36.1±20.9
10-year mortality estimate after CABG, %	29.6±18.4
ARD in 10-year mortality estimates, %*	6.5±4.7

Data are presented as N (%) or mean±SD. * ARD = risk estimate after PCI (%) – risk estimate after CABG (%). ARD: absolute risk difference; BMI: body mass index; CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; LAD: left anterior descending artery; LCx: left circumflex artery; LVEF: left ventricular ejection fraction; MACE: major adverse cardiovascular events; PAD: peripheral artery disease; PCI: percutaneous coronary intervention; RCA: right coronary artery; SD: standard deviation

AGREEMENT OF HEART TEAM TREATMENT RECOMMENDATIONS BETWEEN THE QFR AND FFR APPROACHES

The Heart Teams made treatment recommendations for 248 patients with a full set of QFR and FFR data. **Table 2** shows that the agreement between the Heart Team's treatment recommendations for the QFR and FFR approaches was 91.5% (227/248). The results for all patients are tabulated in **Supplementary Appendix 12**. Cohen's kappa for the agreement in treatment recommendations was 0.73 [95% CI:

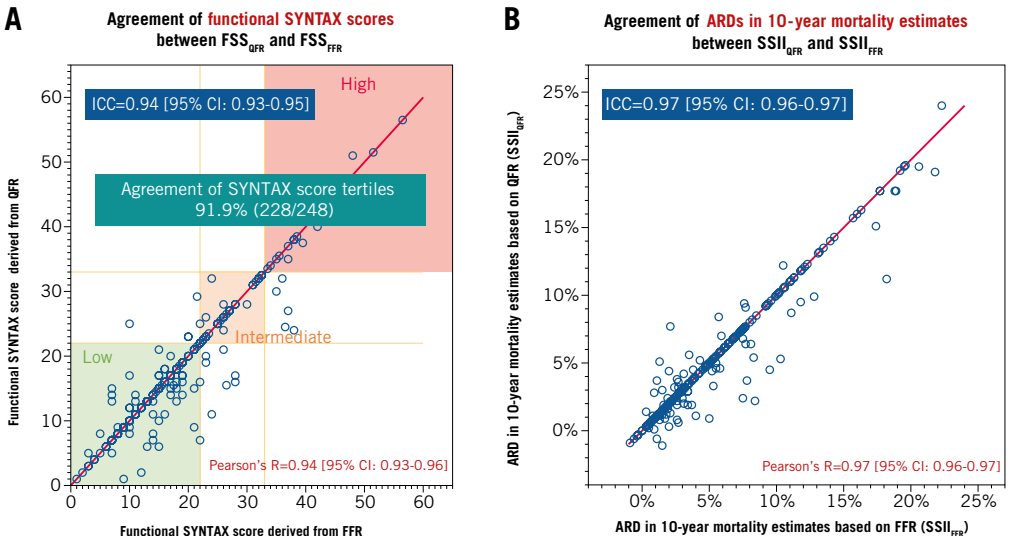


Figure 2. *Agreements in functional SYNTAX scores and absolute risk differences in 10-year mortality estimates derived from the SSII between QFR and FFR. A) When the FSS were stratified into classic categories (low: ≤22, intermediate: 23-32, high: ≥33), the agreement of the categories was 91.9%; (B) the ARD represents an absolute excess mortality risk after PCI treatment compared with CABG treatment (i.e., predicted risk after PCI treatment [%] – predicted risk after CABG treatment [%]) estimated from SSII. ARD: absolute risk difference; CI: confidence interval; FFR: fractional flow reserve; FSS: functional SYNTAX score; ICC: interclass correlation coefficient; QFR: quantitative flow ratio; R: Pearson's correlation coefficient; SSII: SYNTAX score II 2020*

Table 2. Agreement of Heart Team treatment recommendations between QFR and FFR approaches.

		Heart Team treatment recommendation based on QFR-based physiological information		
		PCI/equipoise	**CABG**	
Heart Team treatment recommendation based on FFR-based physiological information	**PCI/equipoise**	76.2% (189/248)	4.4% (11/248)	80.6% (200/248)
	CABG	4.0% (10/248)	15.3% (38/248)	19.4% (48/248)
		80.2% (199/248)	19.8% (49/248)	Agreement 91.5% (227/248)

CABG: coronary artery bypass grafting; FFR: fractional flow reserve; PCI: percutaneous coronary intervention; QFR: quantitative flow ratio

0.62-0.83] **(Figure 3)**. The prespecified kappa goal was 0.60 (lower boundary of 95% CI: 0.40). Therefore, the primary endpoint was achieved.

AGREEMENT OF HEART TEAM REVASCULARISATION PLANNING BETWEEN QFR AND FFR APPROACHES

The two Heart Teams deliberated on the indications for revascularisation in 545 vessels for PCI and 575 for CABG. Regarding the agreement in target vessels for revascularisation between the QFR and FFR approaches, Cohen's kappa was 0.72 [95% CI: 0.66-0.78] in the case of PCI and 0.72 [95% CI: 0.66-0.78] in the case of CABG **(Supplementary Appendix 13)**.

DIFFERENCES IN PATIENT BACKGROUND BETWEEN PATIENTS WITH HEART TEAM DECISION AGREEMENT AND DISAGREEMENT

Of the 248 patients, 21 (8.5%) had discrepancies in the treatment recommendations from the two Heart Teams **(Figure 4)**. Those with decision discrepancies had a higher prevalence of diabetes and peripheral artery disease, as well as higher SSs (anatomical SS and FSS) and estimated ARDs, than those with decision agreement between the two Heart Teams **(Supplementary Appendix 14)**. This suggests that more complex patients (i.e., those more suitable for CABG) were more likely to drive a decision discrepancy between the two Heart Teams. The difference between the predicted ARDs derived from the SSII$_{QFR}$ and SSII$_{FFR}$ was more prominent in the patients for whom the Heart Team's decision was discrepant than for those with matched recommendations (1.39±2.08% vs 0.43±0.98%; p<0.001), suggesting that a greater mismatch between QFR and FFR leads to disparate treatment recommendations.

HEART TEAM TREATMENT RECOMMENDATIONS AFTER UNBLINDING

The Heart Team assigned to the QFR approach changed its treatment recommendations (CABG only, equipoise, and PCI

only) in 21 (8.7%) patients after unblinding the allocation, FFR values, FSS_{FFR}, and $SSII_{FFR}$. After unblinding, Cohen's kappa increased slightly (to 0.76 [95% CI: 0.65-0.86]) with 92.3% agreement. When we evaluated the consistency between the treatment decisions before and after unblinding in the Heart Team using the QFR approach, Cohen's kappa was 0.95 [95% CI: 0.90-1.00].

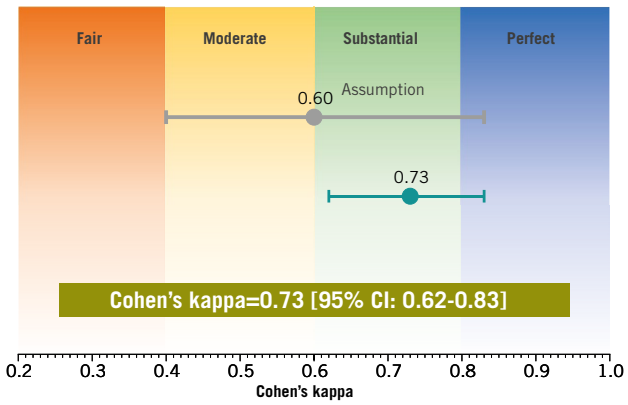


Figure 3. *Level of agreement in the recommended revascularisation mode between the QFR and FFR approaches in the Heart Team discussion as assessed using Cohen's kappa. Cohen's kappa for the agreement in treatment recommendations was 0.73 [95% CI: 0.62-0.83]. The prespecified kappa goal was 0.60, with a lower boundary of the 95% CI of 0.40. The primary endpoint of this trial was achieved. CI: confidence interval; FFR: fractional flow reserve; QFR: quantitative flow ratio*

Discussion

This trial investigated the feasibility of using physiological data based on QFR compared with a physiological assessment with FFR by evaluating Heart Team discussions to determine the recommended revascularisation mode in patients with MVD **(Central illustration)**. The trial showed substantial agreement in the treatment recommendations made by the Heart Teams using QFR or FFR data. The Heart Team assigned to the QFR approach provided consistent recommendations even after being aware of the FFR data. There was substantial agreement in the vessels targeted for revascularisation between the two teams for PCI and CABG. QFR required a significantly shorter procedure time than FFR for measuring the physiological indices of interest.

The RIPCORD 2 trial investigated the impact of a systematic FFR assessment of all relevant coronary arteries (median of four examined vessels) on resource use, quality of life, and clinical outcomes. In that trial, 1.8% of patients experienced complications associated with FFR measurements (coronary dissection, acute myocardial infarction, retained wire elements, and arrhythmia)[16]. Similarly, the current trial included four patients (1.5%) who experienced complications during FFR measurement (1 arrhythmia, 1 hypotension, and 2 wire injuries). In contrast, QFR was developed without the

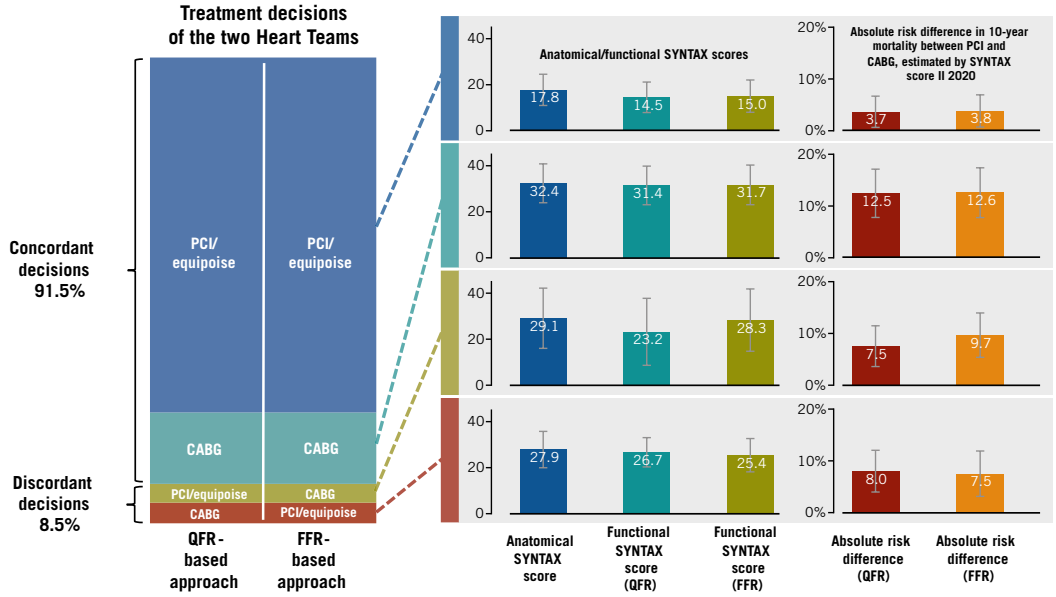


Figure 4. *Relationship between decision concordance and estimated absolute risk differences in 10-year mortality. In cases with decision concordance between QFR and FFR approaches, the functional SYNTAX scores based on QFR and FFR were comparable. Consequently, absolute risk differences (ARDs) for 10-year mortality between PCI and CABG treatments, which were estimated with SYNTAX score II 2020, were also comparable between the two approaches. However, in cases with decision discordance between the two approaches, numerically higher ARDs were observed in the approaches where the Heart Team chose CABG treatment. CABG: coronary artery bypass grafting; FFR: fractional flow reserve; PCI: percutaneous coronary intervention; QFR: quantitative flow ratio*

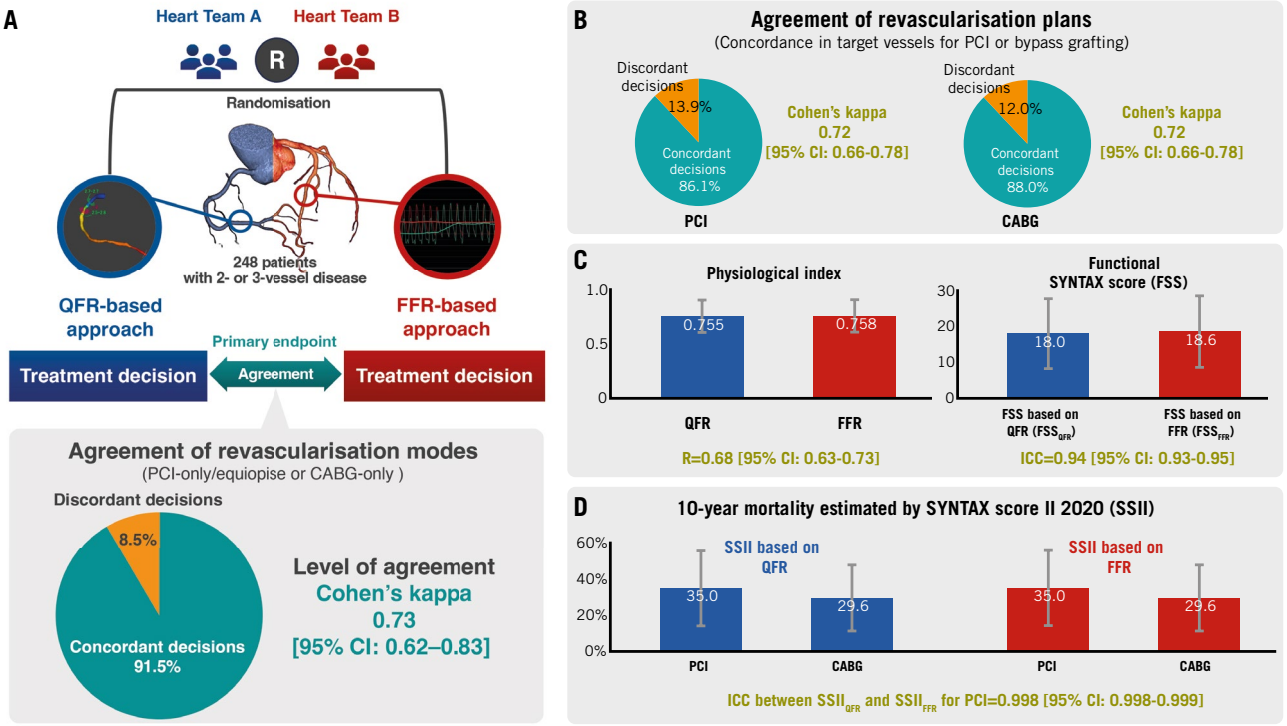
need for a pressure wire or hyperaemia-inducing drugs, thus avoiding these complications[17]. In the current trial, QFR had a shorter procedure time for interrogating coronary lesions than FFR. Furthermore, QFR allows for *post hoc* analysis. Thus, physiological assessment of the vessels of interest by QFR does not require patients to stay in the catheter room for a prolonged period. Wireless functional assessment using QFR may overcome the limitations of the FSS using FFR.

In the *post hoc* study of the SYNTAX II trial investigating the prognostic capability of the FSS_{QFR}, only 28.1% of patients had a full set of analysable QFR in the entire coronary tree, enabling FSS_{QFR} calculation[8]. However, our trial demonstrated a high availability rate of the FSS_{QFR} (98.5%), owing to the substantial analysability of QFR. This suggests that the FSS_{QFR} is feasible if an operator performs angiography by prospectively considering QFR analysis. Interestingly, in the current trial, the prespecified angiographic protocol did not improve the analysability or diagnostic performance of the QFR, although it played an essential role in shortening the analysis time. Cine angiograms with fixed projection angles may reduce the time required to select the exact cine and frame to capture an appropriate angiographic image for QFR analysis.

Notably, even after sharing identical patient data (i.e., unblinding), the two Heart Teams provided unmatched treatment recommendations for 7.7% (19/248) of the patients (Cohen's kappa=0.76). This means that some of the observed disagreements in treatment recommendations could be ascribed to between-team decision variance. However, we consider that this conflict is also associated with the mismatch between QFR and FFR. Patients with unmatched treatment recommendations showed a more significant difference in

EuroIntervention — Central Illustration

The DECISION QFR trial randomised two Heart Teams to either quantitative flow ratio (QFR) or fractional flow reserve (FFR) patient data to determine the optimal revascularisation strategy for 260 patients with multivessel disease.



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The primary interest of the trial was the level of agreement in treatment recommendations made based on QFR or FFR data as assessed with Cohen's kappa (A). There were substantial agreements between vessel-level treatment revascularisation plans made by the two Heart Teams (B). Additionally, QFR yielded comparable physiological indices, functional SYNTAX score (C), and 10-year mortality estimations derived from SYNTAX score II 2020 (D) with FFR. CABG: coronary artery bypass grafting; CI: confidence interval; FFR: fractional flow reserve; ICC: interclass correlation coefficient; MVD: multivessel disease; PCI: percutaneous coronary intervention; QFR: quantitative flow ratio; R: Pearson's correlation coefficient

ARDs between the $SSII_{QFR}$ and $SSII_{FFR}$ than those with matched recommendations **(Figure 4, Supplementary Appendix 14)**. Among the 21 cases where the Heart Team assigned to the QFR approach revised its decisions after unblinding the FFR values, 14 cases (66.7%) exhibited discrepancies in the assessment of the functional significance of the LAD between the QFR and FFR assessments. Additionally, all 21 cases showed differences in the number of functionally significant vessels when comparing the two assessments **(Supplementary Appendix 15)**. However, this trial did not have enough statistical power to enable a causal analysis of the decision discrepancy between the Heart Teams.

Limitations

The current trial is the first to reveal the feasibility of vessel-level wireless physiological assessment using QFR to inform Heart Team discussions. Our results suggest that coronary angiography leading to QFR analysis includes not only anatomical data but also vessel-level physiological data, which can be as valuable as FFR in Heart Team discussions. This study has some limitations. First, it did not investigate the impact of the QFR-based Heart Team treatment decisions on clinical outcomes. Recent studies have generated controversy regarding the significance of physiological evaluations, particularly FFR, in the context of coronary revascularisation[16,17]. Studies evaluating the impact of QFR-guided treatment decisions on patient clinical outcomes in Heart Teams are warranted. Second, the current study has several exclusion criteria related to background and anatomical conditions. Indeed, 28.1% of the screened patients were excluded because they met one or more of these criteria. It is important to recognise that the findings of this study may not be universally applicable in real-world practice. Third, the current trial did not assess the impact of functional information such as QFR and FFR on the Heart Team decisions, as compared with anatomical information only. Fourth, in the current trial, QFR was analysed only in the vessels where FFR was measured. This design may eventually underestimate the clinical advantage of QFR, because QFR can be potentially analysed in the vessels where FFR cannot be measured due to anatomical issues which increase the risk of the pressure wire manipulation. Fifth, the QFR analysis in this trial was conducted by experienced operators. It has been reported that the accuracy and reproducibility of QFR analysis were associated with the experience of the operator[18]. Sixth, in the secondary endpoint analysis for the agreement of vessel-level treatment decisions for each patient between the two Heart Teams, the nested structure within each patient could be reasonable for the calculation of Cohen's kappa. However, this modification potentially causes the results to be interpreted as complex, because this modification is not generally employed.

Conclusions

In Heart Team discussions for determining the optimal revascularisation mode in candidates with MVD, QFR provided comparable physiological data to FFR. This allowed for a non-invasive assessment of the functional significance of coronary artery stenosis on angiography, enabling determination of the most suitable treatment.

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Funding

The current investigator-initiated trial received a national Grant-in-Aid for Scientific Research (19K17617).

Conflict of interest statement

J.H.C. Reiber is the CSO of Medis Medical Imaging Systems and has a part-time appointment at Leiden University Medical Center as a Professor of Medical Imaging. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix 1. Inclusion and exclusion criteria of the trial.

Supplementary Appendix 2. Participating sites.

Supplementary Appendix 3. Prespecified angiographic projection angles.

Supplementary Appendix 4. Treatment recommendations in the virtual Heart Team discussion.

Supplementary Appendix 5. Study flowchart of the DECISION QFR trial.

Supplementary Appendix 6. Reasons for excluding patients in the eligibility assessment.

Supplementary Appendix 7. Analysis flowchart of FFR and QFR.

Supplementary Appendix 8. Comparison in procedure time between QFR and FFR measurements in all patients (A) and patients undergoing angiography with the prespecified angiographic projection angles (B).

Supplementary Appendix 9. Comparison in procedure time between QFR and FFR measurements in patients with CIV (A) and patients with IC (B).

Supplementary Appendix 10. Comparison in procedure time between QFR and FFR measurements in patients with CIV (A) and patients with IC (B).

Supplementary Appendix 11. Summary table of QFR/FFR, functional SYNTAX score, and SYNTAX score II 2020 based on QFR/FFR.

Supplementary Appendix 12. The results of all Heart Team discussions in the trial.

Supplementary Appendix 13. Agreement of revascularisation target vessels in PCI (A) and CABG (B) treatments between QFR and FFR approaches.

Supplementary Appendix 14. Differences in the patient background between patients with Heart Team decision agreement and disagreement.

Supplementary Appendix 15. Details of the Heart Team decisions and differences between QFR-based and FFR-based assessments in the 21 patients.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-23-00674

Supplementary data

Supplementary Appendix 1. Inclusion and exclusion criteria of the trial.

The current trial enrolled the patients with (1) chronic coronary syndrome requiring revascularization (PCI or CABG); and (2) multiple lesions with DS of ≥50% (visual assessment) located in ≥2 vessels including the proximal left anterior descending (SYNTAX score segment: 6 and/or 7).

The exclusion criteria of the trial were as follows: (1) left main coronary artery lesion or ostial lesion of right coronary artery disease that is not recommended for the QFR analysis; (2) history of CABG; (3) advanced chronic kidney disease (estimated GFR <30 ml/min/1.73 m2) or receiving hemodialysis; (4) atrial fibrillation at the time of angiography; (5) severe valvular diseases; and (6) heart failure requiring oxygen supply.

Supplementary Appendix 2. Participating sites.

1. Sapporo Higashi Tokushukai Hospital, Sapporo, Japan
2. Tsuchiura Kyodo General Hospital, Ibaraki, Japan
3. Mitsui Memorial Hospital, Tokyo, Japan
4. St. Luke's International Hospital, Tokyo, Japan
5. Toho University Ohashi Medical Center, Japan
6. Gifu Heart Centre, Gifu, Japan
7. Osaka Police Hospital, Osaka, Japan
8. Wakayama Medical University, Wakayama, Japan
9. Yamaguchi University, Yamaguchi, Japan
10. Kokura Memorial Hospital, Kitakyushu, Japan

Supplementary Appendix 3. Prespecified angiographic projection angle.

Right coronary artery	Left coronary arteries
LAO45°, CAUD10°	LAO30°, CRAN30°
LAO20°, CRAN20°	AP, CRAN45°
RAO30°, CAUD20°	RAO30°, CRAN20°
	RAO25°, CAUD25°
	RAO20°, CAUD45°
	AP, CAUD10°
	LAO10°, CAUD25°

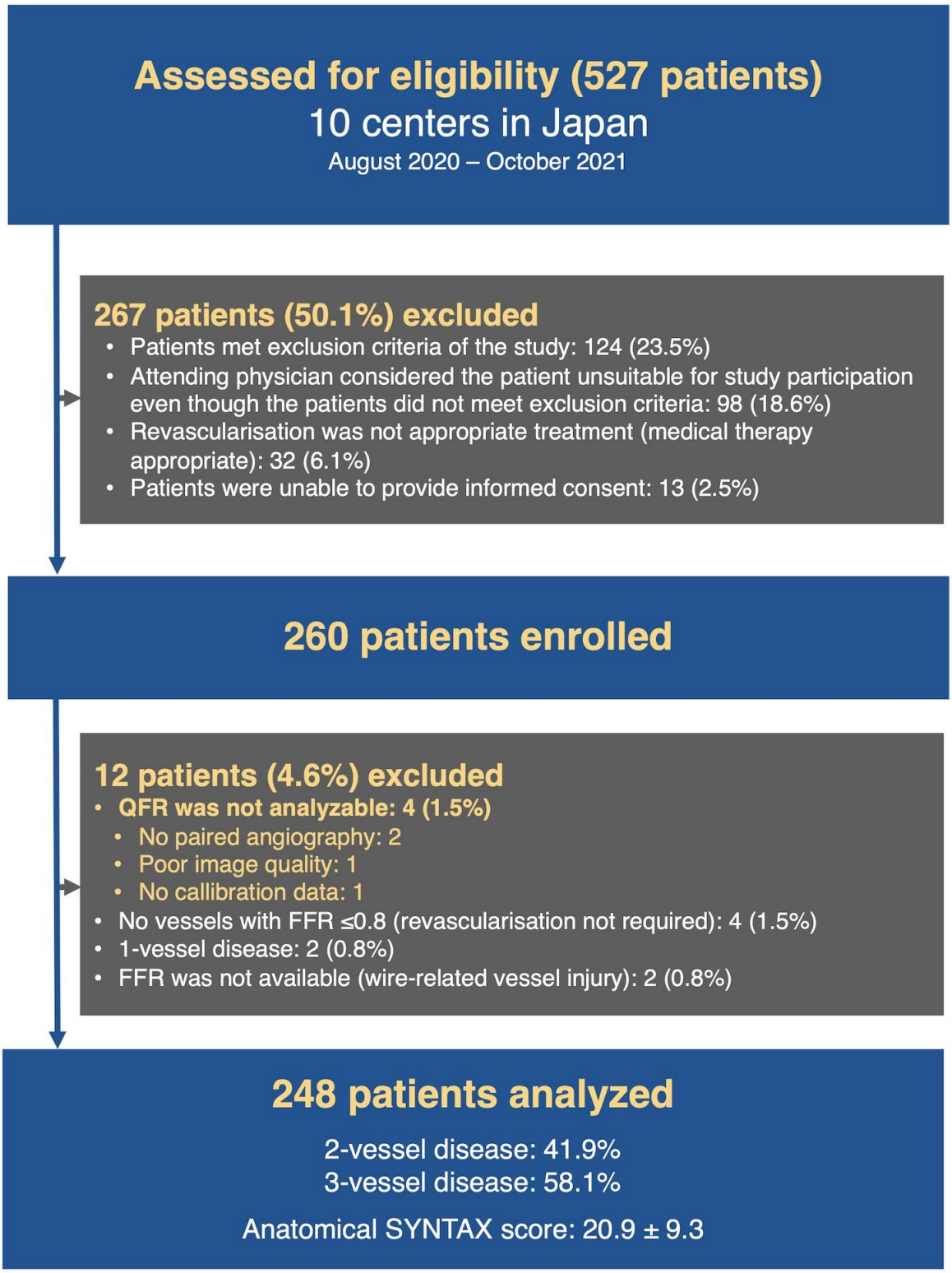
Supplementary Appendix 4. Treatment recommendation in the virtual Heart Team discussion.

1) CABG only. The patient is recommended to receive CABG because the benefit of CABG is highlighted according to the risk assessment using (anatomical and functional) SS and SSII.

2) Equipoise. The patient is recommended to receive either CABG or PCI because the benefit of each treatment is equipoised according to the risk assessment using (anatomical and functional) SS and SSII.

3) PCI only. The patient is recommended to receive PCI because the benefit of PCI is highlighted according to the risk assessment using (anatomical and functional) SS and SSII.

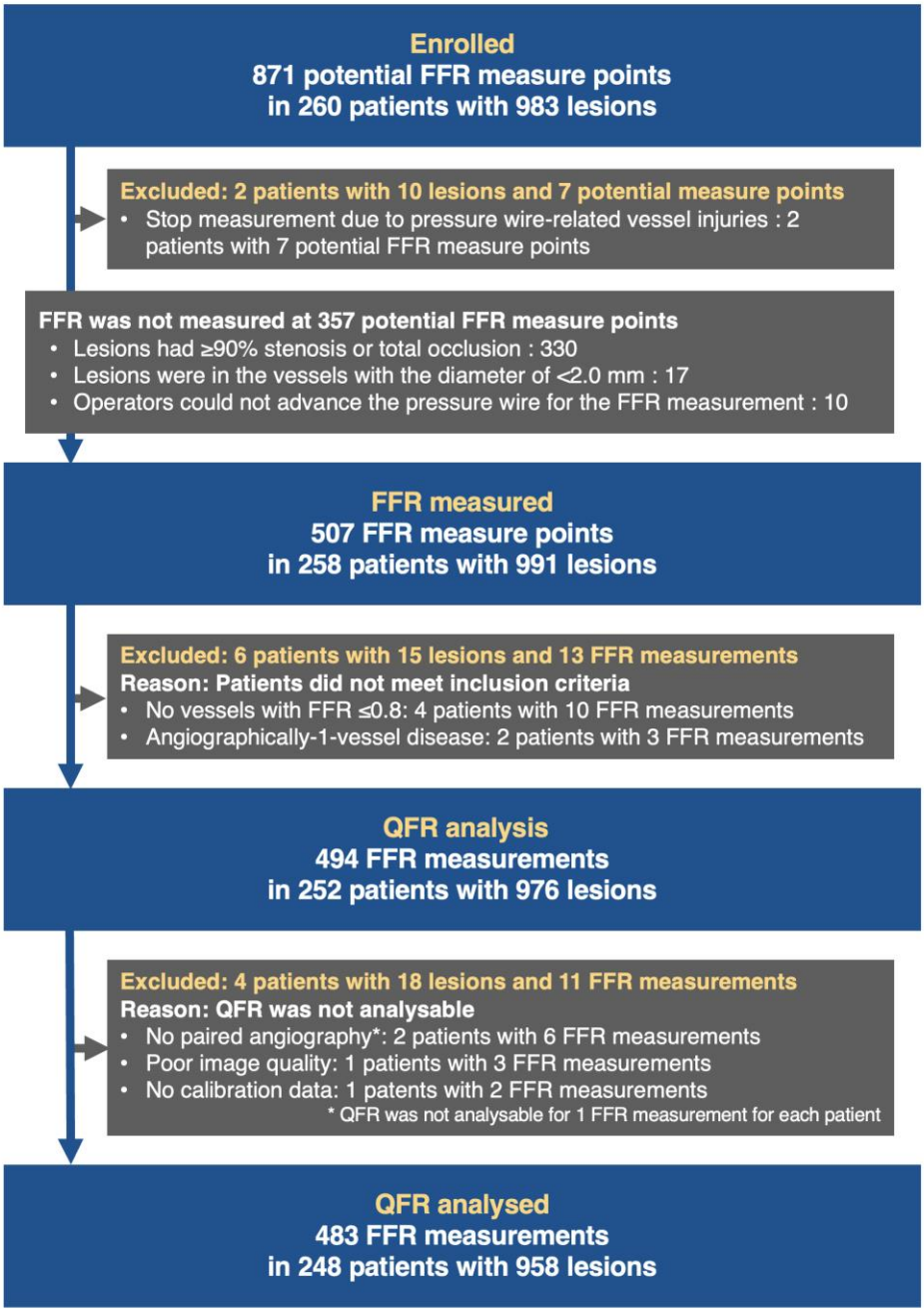
Supplementary Appendix 5. Study flowchart of the DECISION QFR trial.



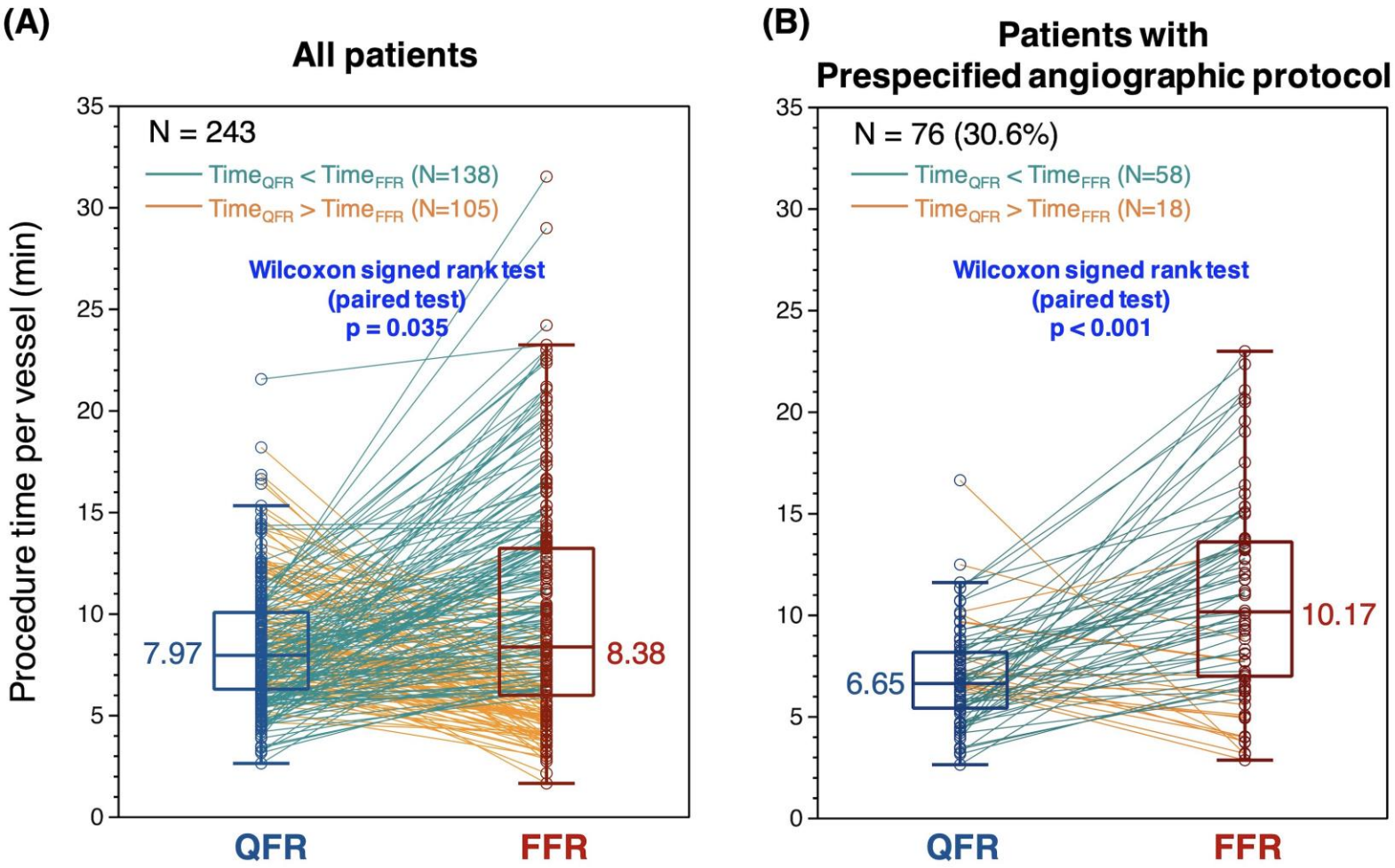
Supplementary Appendix 6. Reasons for excluding patients in the eligibility assessment.

Reasons for exclusion	Number
Excluded after eligibility assessment	
Patients were unable to provide informed consent	13
Patients where revascularisation was not appropriate as treatment (medical therapy appropriate)	26
Patients where the attending physician deemed the patient unsuitable for participation in the study	98
Patients with lesions in the left main trunk and the entrance of the right coronary artery (3mm)	12
Patients who underwent CABG surgery	31
Patients with chronic kidney disease with eGFR <30 ml/min/1.73m² and dialysis patients	25
Patients with atrial fibrillation	29
Patients with severe valve disease	10
Patients with heart failure requiring oxygen therapy	5
Pre-registored with concent but excluded after coronary angiography	
Patients with lesions in the left main trunk and the entrance of the right coronary artery (3mm)	11
Patients where revascularisation was not appropriate as treatment (medical therapy appropriate)	6
Patients with atrial fibrillation during coronary angiography	1
Total	**267**

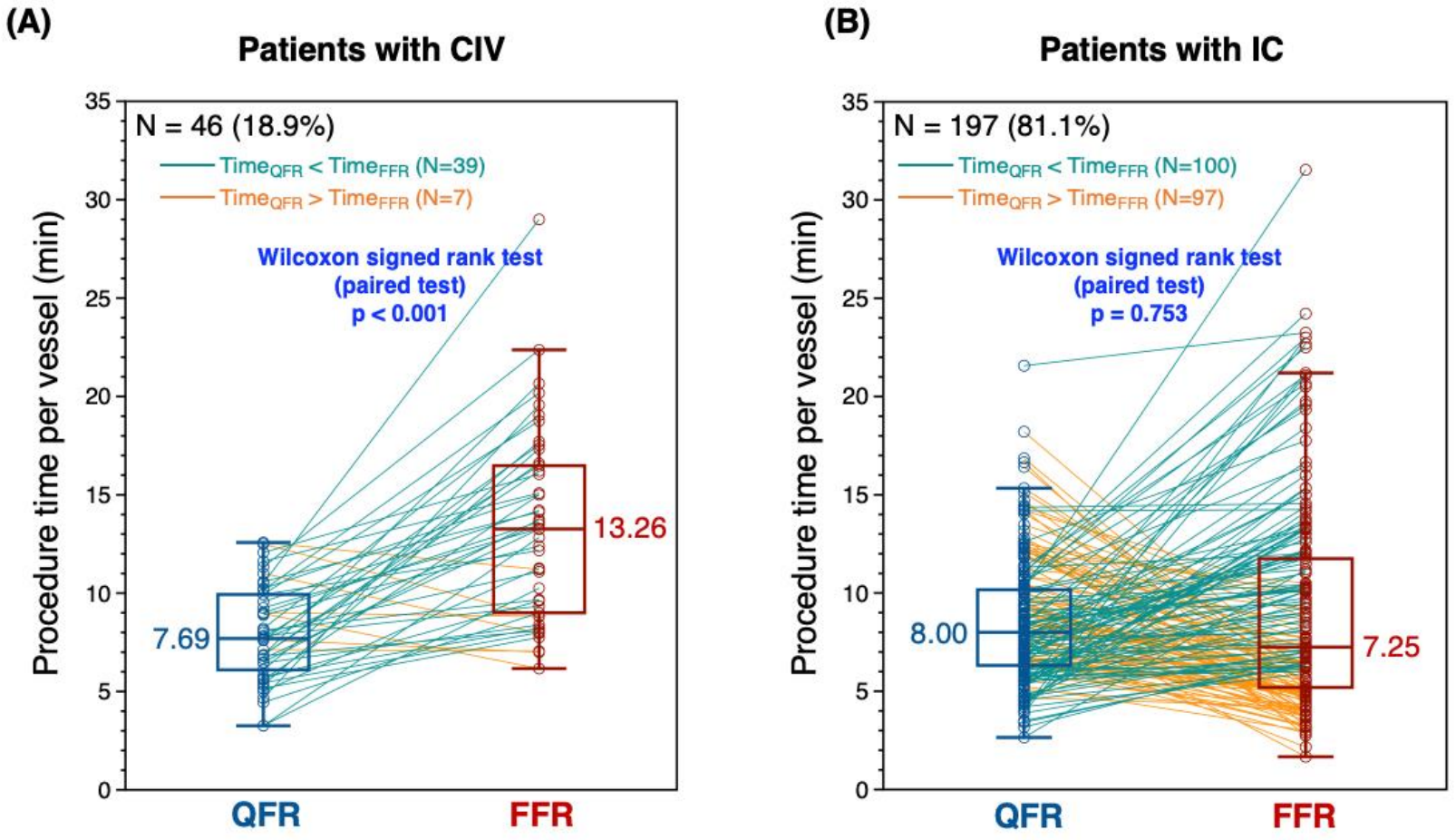
Supplementary Appendix 7. Analysis flow chart of FFR and QFR.



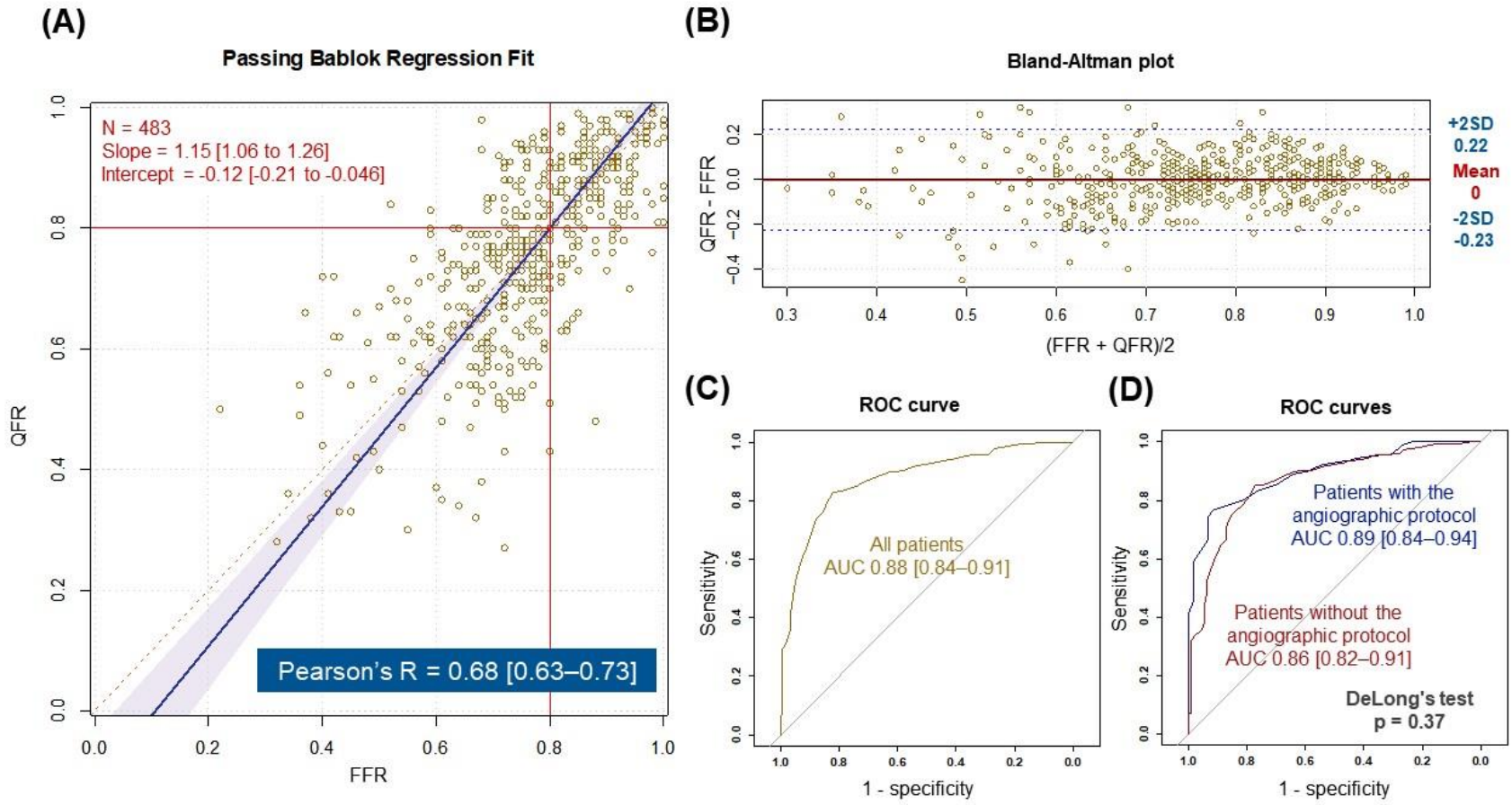
Supplementary Appendix 8. Comparison in procedure time between QFR and FFR measurements in all patients (A) and patients undergoing angiography with the prespecified angiographic projection angles (B).



Supplementary Appendix 9. Comparison in procedure time between QFR and FFR measurements in patients with CIV (A) and patients with IC (B).



10. Supplementary Appendix 10.



Supplementary Appendix 11. Summary table of QFR/FFR, functional SYNTAX score, and SYNTAX score II 2020 based on QFR/FFR.

	QFR	FFR
	Median (IQR)	Median (IQR)
	N = 483 vessels	
Value of physiological index	0.77 (0.67–0.87)	0.76 (0.69–0.85)
Procedure time per vessel (min)†	7.97 (6.30–10.08)	8.38 (6.00–13.23)
Only patients undergoing angiography with the prespecified angiographic protocol (N = 76 patients, 149 vessels)††	6.65 (5.47–8.18)	10.17 (7.03–13.59)
	Mean ± SD	Mean ± SD
	N = 248 patients	
Functional SYNTAX score	18.0 ± 9.7	18.6 ± 10
SYNTAX score II 2020 based on physiological index		
5-year MACE estimate after PCI (%)	24.4 ± 14	24.6 ± 14
5-year MACE estimate after CABG (%)	19.0 ± 10.4	19.0 ± 10.4
ARD in 5-year MACE estimates (%)*	5.3 ± 5.1	5.5 ± 5.2
10-year mortality estimate after PCI (%)	35.0 ± 20.8	35.2 ± 20.9
10-year mortality estimate after CABG (%)	29.6 ± 18.3	29.6 ± 18.3
ARD in 10-year mortality estimates (%)*	5.4 ± 4.7	5.6 ± 4.8

MACE: major adverse cardiovascular event, PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft, ARD: absolute risk difference, SD: standard deviation.
†p = 0.035 with Wilcoxon signed-rank test
††p < 0.001 with Wilcoxon signed-rank test
*ARD: risk estimate after PCI (%) – risk estimate after CABG

Supplementary Appendix 12. The results of all Heart Team discussions in the trial.

E00001	CABG	E00023	PCI or CABG	E00044	PCI or CABG	E00065	PCI or CABG	E00087	PCI or CABG	E00108	PCI or CABG	E00130	PCI or CABG	E00152	PCI or CABG	E00174	PCI or CABG	E00196	PCI or CABG	E00220	PCI or CABG	E00243	PCI or CABG
	Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG
E00002	PCI or CABG	E00024	CABG	E00045	PCI	E00066	PCI or CABG	E00088	PCI or CABG	E00109	PCI	E00131	PCI or CABG	E00153	PCI or CABG	E00175	PCI or CABG	E00197	CABG	E00221	PCI or CABG	E00244	PCI
	Agreement		Agreement		Agreement		Agreement		Agreement		Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	PCI or CABG		CABG		PCI		PCI		PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG		PCI
E00004	PCI or CABG	E00025	PCI or CABG	E00046	PCI	E00067	PCI	E00089	PCI or CABG	E00110	PCI	E00132	CABG	E00154	PCI or CABG	E00176	PCI or CABG	E00198	PCI or CABG	E00223	CABG	E00245	PCI or CABG
	Agreement		Agreement		Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	PCI or CABG		PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG
E00005	PCI or CABG	E00026	PCI or CABG	E00047	PCI or CABG	E00068	PCI or CABG	E00090	PCI or CABG	E00111	PCI or CABG	E00133	PCI or CABG	E00155	PCI or CABG	E00177	PCI	E00199	CABG	E00224	PCI or CABG	E00247	PCI
	Agreement		Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG		PCI
E00006	CABG	E00027	PCI or CABG	E00048	CABG	E00069	PCI	E00091	PCI or CABG	E00112	CABG	E00134	CABG	E00156	PCI or CABG	E00178	PCI or CABG	E00200	PCI or CABG	E00225	PCI or CABG	E00248	PCI or CABG
	Agreement		Agreement		Agreement		Agreement		Agreement		Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	CABG		PCI		CABG		PCI		PCI or CABG		PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG
E00007	PCI or CABG	E00028	PCI or CABG	E00049	PCI or CABG	E00070	PCI or CABG	E00092	CABG	E00113	PCI or CABG	E00135	PCI or CABG	E00157	PCI or CABG	E00179	PCI or CABG	E00201	PCI	E00226	CABG	E00250	PCI or CABG
	Agreement		Agreement		Agreement		Agreement		Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG
E00008	PCI or CABG	E00029	CABG	E00050	PCI	E00071	PCI or CABG	E00093	CABG	E00114	PCI or CABG	E00136	PCI or CABG	E00158	PCI or CABG	E00180	CABG	E00202	PCI or CABG	E00227	PCI or CABG	E00251	PCI or CABG
	Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	PCI or CABG		CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG
E00009	PCI	E00030	PCI	E00051	PCI	E00072	CABG	E00094	PCI or CABG	E00115	PCI or CABG	E00137	PCI or CABG	E00159	PCI or CABG	E00181	CABG	E00203	PCI or CABG	E00228	PCI or CABG	E00252	PCI or CABG
	Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	PCI or CABG		PCI or CABG		PCI		CABG		PCI		PCI or CABG		PCI		PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG
E00010	PCI or CABG	E00031	PCI or CABG	E00052	PCI	E00073	CABG	E00095	PCI or CABG	E00116	PCI	E00138	PCI	E00160	PCI or CABG	E00182	PCI	E00204	PCI or CABG	E00229	PCI or CABG	E00253	CABG
	Agreement		Agreement		Agreement		Agreement		Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	PCI or CABG		PCI or CABG		PCI		CABG		CABG		PCI		PCI		PCI		PCI		PCI or CABG		PCI or CABG		CABG
E00011	PCI or CABG	E00032	PCI or CABG	E00053	PCI or CABG	E00074	PCI	E00096	CABG	E00117	PCI or CABG	E00139	PCI or CABG	E00161	PCI	E00183	PCI or CABG	E00205	PCI or CABG	E00230	CABG	E00254	PCI or CABG
	Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Disagreement		Agreement		Agreement		Agreement
	PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG		CABG		PCI or CABG
E00012	PCI or CABG	E00033	PCI or CABG	E00054	PCI or CABG	E00075	PCI or CABG	E00097	PCI	E00118	PCI or CABG	E00140	PCI or CABG	E00162	PCI or CABG	E00184	PCI or CABG	E00206	PCI or CABG	E00231	PCI or CABG	E00255	PCI or CABG
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	PCI or CABG		PCI		PCI or CABG		PCI or CABG		PCI		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG
E00013	PCI or CABG	E00034	PCI	E00055	PCI or CABG	E00077	CABG	E00098	PCI or CABG	E00119	CABG	E00141	CABG	E00163	PCI or CABG	E00185	CABG	E00207	PCI or CABG	E00233	PCI	E00256	PCI or CABG
	Agreement		Agreement		Agreement		Disagreement		Agreement		Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG		CABG		PCI		PCI or CABG		PCI
E00014	PCI or CABG	E00035	CABG	E00056	PCI or CABG	E00078	PCI	E00099	PCI or CABG	E00120	PCI or CABG	E00143	PCI	E00164	PCI or CABG	E00186	PCI	E00208	PCI or CABG	E00234	PCI or CABG	E00257	PCI or CABG
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	PCI or CABG		CABG		PCI or CABG		PCI		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI		PCI or CABG
E00015	CABG	E00036	PCI or CABG	E00057	PCI or CABG	E00079	PCI	E00100	PCI	E00122	PCI or CABG	E00144	PCI or CABG	E00165	PCI or CABG	E00187	PCI or CABG	E00210	PCI or CABG	E00235	CABG	E00258	PCI or CABG
	Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	CABG		PCI or CABG		PCI or CABG		PCI		PCI		PCI or CABG		PCI		PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG
E00016	CABG	E00037	CABG	E00058	PCI or CABG	E00080	PCI or CABG	E00101	CABG	E00123	CABG	E00145	PCI or CABG	E00166	CABG	E00188	PCI or CABG	E00211	PCI or CABG	E00236	PCI	E00259	PCI or CABG
	Agreement		Disagreement		Agreement		Agreement		Agreement		Disagreement		Disagreement		Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement
	CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI
E00017	PCI or CABG	E00038	PCI	E00059	PCI or CABG	E00081	PCI	E00102	CABG	E00124	PCI or CABG	E00146	CABG	E00167	PCI	E00189	PCI or CABG	E00212	CABG	E00237	PCI or CABG	E00260	PCI or CABG
	Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Disagreement		Agreement		Agreement
	PCI or CABG		PCI		PCI or CABG		PCI		CABG		PCI or CABG		CABG		PCI		PCI or CABG		CABG		CABG		PCI or CABG
E00018	CABG	E00039	PCI	E00060	PCI	E00082	PCI or CABG	E00103	PCI	E00125	PCI or CABG	E00147	PCI or CABG	E00169	PCI or CABG	E00190	PCI or CABG	E00213	CABG	E00238	CABG	E00261	PCI
	Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement
	PCI or CABG		PCI		PCI		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		CABG		PCI or CABG
E00019	PCI or CABG	E00040	PCI or CABG	E00061	PCI or CABG	E00083	PCI or CABG	E00104	PCI or CABG	E00126	PCI or CABG	E00148	PCI	E00170	PCI or CABG	E00191	PCI	E00214	CABG	E00239	PCI or CABG		
	Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		
	PCI or CABG		PCI		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI		PCI or CABG		PCI or CABG		CABG		PCI or CABG		
E00020	PCI or CABG	E00041	PCI or CABG	E00062	PCI or CABG	E00084	CABG	E00105	CABG	E00127	CABG	E00149	PCI or CABG	E00171	CABG	E00192	PCI or CABG	E00215	PCI or CABG	E00240	PCI or CABG		
	Disagreement		Agreement		Agreement		Agreement		Agreement		Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement				
	CABG		PCI or CABG		PCI or CABG		CABG		CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG		
E00021	PCI or CABG	E00042	PCI or CABG	E00063	PCI or CABG	E00085	PCI or CABG	E00106	PCI or CABG	E00128	CABG	E00150	PCI or CABG	E00172	PCI or CABG	E00193	PCI or CABG	E00218	CABG	E00241	CABG		
	Agreement		Agreement		Agreement		Disagreement		Agreement		Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement				
	PCI or CABG		PCI or CABG		PCI or CABG		CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		CABG		CABG		
E00022	CABG	E00043	PCI	E00064	CABG	E00086	PCI or CABG	E00107	PCI or CABG	E00129	PCI or CABG	E00151	PCI or CABG	E00173	PCI or CABG	E00195	PCI or CABG	E00219	PCI	E00242	PCI or CABG		
	Agreement		Agreement		Disagreement		Agreement		Agreement		Agreement		Agreement		Agreement		Agreement		Disagreement		Agreement				
	CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI or CABG		PCI		PCI or CABG		CABG		PCI or CABG		

Legend

E000xx

QFR-based decision

Agreement

FFR-based decision

Supplementary Appendix 13. Agreement of revascularisation target vessels in PCI (A) and CABG (B) treatments between QFR and FFR approaches.

(A)

		Heart Team treatment recommendation based on QFR-based physiological information		
		Yes	No	
Heart Team treatment recommendation based on FFR-based physiological information	Yes	47.3% (258/545)	5.9% (32/545)	53.2% (290/545)
	No	8.1% (44/545)	38.7% (211/545)	46.8% (255/545)
		55.4% (302/545)	44.6% (243/545)	Agreement 86.1% (469/545)

(B)

		Heart Team treatment recommendation based on QFR-based physiological information		
		Yes	No	
Heart Team treatment recommendation based on FFR-based physiological information	Yes	63.0% (362/575)	5.7% (33/575)	68.7% (395/575)
	No	6.3% (36/575)	25.0% (144/575)	31.3% (180/575)
		69.2% (398/575)	30.8% (177/575)	Agreement 88.0% (506/575)

Supplementary Appendix 14. Differences in the patient background between patients with Heart Team decision agreement and disagreement.

	Patients with Heart Team decision agreement	Patients with Heart Team decision disagreement	p value
	N = 227	N = 21	
Age (y)	70.89±10.20	69.38±10.14	0.516
Male	179 (78.9%)	16 (76.2%)	0.995
Hypertention	182 (80.2%)	19 (90.5%)	0.389
Diabetes mellitus	104 (45.8%)	16 (76.2%)	0.015
Dyslipidemia	176 (77.5%)	17 (81.0%)	0.931
Peripheral artery disease	12 (5.3%)	4 (19.0%)	0.046
COPD	7 (3.1%)	0 (0.0%)	0.898
LVEF (%)	59.24±11.87	59.46±11.72	0.934
Hemoglobin (g/dL)	13.82±1.78	14.01±2.47	0.657
Creatinine (mg/dL)	0.94±0.55	0.98±0.28	0.736
Number of lesions	3.78±1.35	4.86±1.96	0.001
Incidence of mismatch in funcional significance between QFR and FFR	15 (7.8%)	3 (15.0%)	0.499
Anatomical SYNTAX score	20.21±8.94	28.45±10.42	<0.001
Functional SYNTAX score based on QFR	17.36±9.39	25.02±10.90	0.001
Functional SYNTAX score based on FFR	17.83±9.58	26.79±10.53	<0.001
ARD in 5-MACE estimate (%)*			
SSII based on angiography	6.13±5.21	8.54±3.83	0.040
SSII based on QFR	5.13±5.16	7.23±3.51	0.069
SSII based on FFR	5.29±5.20	7.93±3.97	0.024
ARD in 10-year mortality estimate (%)*			
SSII based on angiography	6.20±4.66	9.23±4.26	0.004
SSII based on QFR	5.14±4.68	7.79±3.89	0.013
SSII based on FFR	5.29±4.75	8.54±4.37	0.003

COPD: chronic obstructive pulmonary disease, LVEF: left ventricular ejection fraction, QFR: quantitative flow ratio, FFR: fractional flow reserve, PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft, ARD: absolute risk difference.
*ARD: risk estimate after PCI (%) – risk estimate after CABG (%)

Supplementary Appendix 15. Details of the Heart Team decisions and differences between QFR-based and FFR-based assessments in the 21 patients.

Case	Blinded decision of QFR-based approach	Unblinded decision of QFR-based approach	Difference in FSS (FSS_{QFR} - FSS_{FFR})	Difference in SSII for PCI regarding 10-year mortality ($SSII_{QFR}$ - $SSII_{FFR}$)	Discrepancy in LAD functional significance between QFR and FFR	Difference in number of functionally significant vessels (QFR vs FFR)
1	CABG only	PCI or CABG	8	2.7	NO	2 vs 1
2	PCI only	PCI or CABG	-9	-0.8	YES	1 vs 2
3	PCI or CABG	PCI only	7	2.4	YES	2 vs 1
4	PCI only	PCI or CABG	-11	-5	YES	1 vs 2
5	PCI only	PCI or CABG	-11	-4.1	YES	2 vs 3
6	PCI only	PCI or CABG	-13	-5.1	YES	1 vs 2
7	PCI or CABG	PCI only	3	1.1	NO	2 vs 1
8	PCI only	PCI or CABG	-12	-2.9	YES	2 vs 3
9	PCI only	CABG only	-12	-7	YES	2 vs 3
10	PCI only	PCI or CABG	-12	-5	YES	2 vs 3
11	CABG only	PCI or CABG	3	1.8	NO	3 vs 2
12	CABG only	PCI or CABG	3	1.4	NO	2 vs 1
13	PCI or CABG	PCI only	8	3.8	YES	3 vs 2
14	PCI only	PCI or CABG	-7	-2.1	YES	1 vs 2
15	PCI only	PCI or CABG	-1	-0.3	NO	1 vs 2
16	PCI only	PCI or CABG	-6	-4.1	YES	2 vs 3
17	PCI only	PCI or CABG	-15	-6.2	YES	1 vs 2
18	PCI only	PCI or CABG	5	-1.7	NO	1 vs 3
19	PCI or CABG	PCI only	15	5.6	YES	3 vs 1

20	PCI only	PCI or CABG	-7	-1.8	NO	2 vs 3
21	PCI only	PCI or CABG	-5	-1.8	YES	2 vs 3