# **Randomized Comparison of Fractional Flow Reserve and Instantaneous Wave Free Ratio in Serial Disease**

Brief Title: FFR versus iFR in serial disease  
Running Title: FFR versus iFR in serial disease

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The first randomized, within patient comparison of FFR and iFR in serial #CAD shows that both FFR and iFR pullbacks overestimate the hemodynamic benefits of #PCI. Post-PCI physiology should be routinely performed in diffuse and serial disease.

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## Abstract

**Background**

Fractional flow reserve (FFR) and the instantaneous wave-free ratio (iFR) identify arteries that benefit from percutaneous coronary intervention (PCI). FFR or iFR gradients on pullback are often used to predict the physiological result (FFRΔ or iFRΔ), but this approach is unvalidated.

**Objectives**

To compare the accuracy of FFRΔ, iFRΔ and FFRcalc (a mathematical solution incorporating interaction between lesions) for predicting post-PCI physiology in serial/diffuse disease.

**Methods**

Patients with a focal target lesion and either a second focal lesion or diffusely diseased segment in the same vessel were randomized to FFR- versus iFR-guided PCI (ISRCTN18106869). FFR and iFR pullbacks were performed, with operators blinded to one modality. Following target lesion PCI, FFR and iFR were remeasured. The primary outcome was the error in predicted post-PCI physiology compared to actual values. Data are median (IQR).

**Results**

We randomized 87 patients to FFR (n=45) or iFR (n=42). FFR and iFR were 0.70 (0.62 to 0.78) and 0.81 (0.68 to 0.90) at baseline and 0.82 (0.74 to 0.87) and 0.89 (0.83 to 0.93) after target lesion PCI. The predictive errors were 12% (6 to 17%) for FFRΔ, 4% (0 to 9%, p<0.001) for iFRΔ, and -5% (-18 to 8%, p=0.427) for FFRcalc. Significant residual disease was missed in 36% of cases with FFRΔ, 34% with iFRΔ and 14% with FFRcalc.

**Conclusions**

FFR and iFR pullback gradients overestimate the benefit of target-lesion PCI and can miss residual ischemia in a third of patients. FFR or iFR should be routinely repeated post-PCI in serial disease.

## Condensed Abstract

Fractional flow reserve and instantaneous wave free ratio gradients across target lesions are commonly used to predict physiology after percutaneous coronary intervention (FFRΔ and iFRΔ). In 87 patients with serial disease randomized to FFR versus iFR guidance, we compared FFRΔ, iFRΔ and FFRcalc (a mathematical solution that accounts for hemodynamic interaction between serial lesions during hyperemia). Median FFRΔ error was 12%, iFRΔ 4% and FFRcalc -5%. Significant residual disease was missed in 36% by FFRΔ, 34% by iFRΔ and 14% by FFRcalc.FFRcalc shows promise over conventional methods, but for now the direct measurement of post-PCI physiology is strongly recommended.

## Key Words

Percutaneous coronary intervention

Coronary physiology

Fractional flow reserve

Instantaneous wave free ratio

## Abbreviations and Acronyms

CABG Coronary artery bypass grafting

CAD Coronary artery disease

FFR Fractional flow reserve

iFR Instantaneous wave free ratio

PCI Percutaneous coronary intervention

PPG Pressure pullback gradient

SERIAL Systematic Evaluation by Randomisation of Intracoronary physiological techniques for Assessing tandem Lesions

## Introduction

Physiology-guided coronary revascularization in stable coronary artery disease (CAD) improves patient outcomes and reduces costs compared with angiography guidance alone.1–3 However, residual gradients after PCI remain common4,5 and are associated with both persistent angina and long term adverse events.6,7 Contemporary physiological assessment has therefore evolved to characterize the pattern of disease within an artery by performing a pullback of the pressure wire, in order to inform the revascularization strategy and anticipate the likely benefits from PCI.8–10 This is most commonly done by visualizing the intra-coronary pressure pullback trace during pharmacological hyperemia (fractional flow reserve, FFR) or without hyperemia (instantaneous wave free ratio, iFR) and using the gradient across a lesion (dFFR or diFR) to predict the physiological impact of treating that lesion by PCI. The assumption inherent in this approach is that the whole vessel FFR/iFR will increase by a value corresponding to dFFR/diFR.

However, the validity of this assumption and accuracy of this approach have not been systematically evaluated. This is particularly pertinent in arteries with serial lesions and/or diffuse disease, where it can be difficult to predict post-PCI physiology11,12 as the pressure gradient across a proximal stenosis is affected by resistance from a distal stenosis, and vice versa.11 Recently, a mathematical calculation has been described that accounts for the hemodynamic interaction between diseased segments during hyperemia (FFRcalc) and has shown promising results in a single center validation study.12 The primary aim of our study was therefore to compare the accuracy of using dFFR and diFR for predicting the physiological result after PCI to a single target lesion, in coronary arteries with serial disease. Our secondary aim was to evaluate whether the novel parameter, FFRcalc, is associated with less error in predicting the final FFR/iFR compared to the trans-lesional gradients currently used in clinical practice.

## Methods

**Study Design**

SERIAL (Systematic Evaluation by Randomisation of Intracoronary physiological techniques for Assessing tandem Lesions) is a prospective, blinded, randomized controlled trial conducted at 4 centers in the United Kingdom (ISRCTN18106869).

The study was approved by the National Health Service Health Research Authority in the United Kingdom (21/WA/0238) and all participants provided written informed consent. The study was overseen by an independent steering committee, coordinated by the King’s College London Clinical Trials Unit and funded by an unrestricted educational grant from Abbott Vascular. The funder had no role in the design of the trial, data analysis, or decision to submit for publication. Angiographic and physiological data were analyzed by an independent core laboratory at King’s College London blinded to treatment assignments and clinical outcomes. The authors vouch for the accuracy and completeness of the data and analyses, and for fidelity to the trial protocol and statistical analysis plan.

**Participants and Randomization**

Participants were eligible for inclusion if they had a focal lesion on coronary angiography causing ≥50% diameter stenosis by visual estimation, with either a second focal stenosis (that the operator would consider treating with separate non-overlapping stents) or a segment of diffuse disease. Exclusion criteria were if the target vessel was considered culprit for an acute coronary syndrome <72 hours prior to consent, an index STEMI procedure, a target vessel protected by a coronary artery bypass graft, patients <18 years old, inability to provide written informed consent, and pregnancy or breastfeeding at the time of randomization. Eligible patients were randomized 1:1 to an FFR-guided or iFR-guided management strategy. The randomization sequence was computer generated with random block sizes and stratified by age and sex.

**Study Procedures and Blinding**

Participants underwent physiological assessment with FFR and iFR before and after treatment of a single lesion by PCI (Figure 1). Throughout the case, the operator was blinded to the data from one modality according to the randomized treatment assignment. These data were only visible to a member of the research team who advised the operator on the technical quality of the pressure trace and ensured standardized physiological measurements.

Pressure wire assessment was performed according to a standard operating procedure specified in the trial protocol (Supplementary figure S1). Pre-PCI FFR was measured using the PressureWire X (Abbott Laboratories, IL, USA) and pre-PCI iFR was measured using the Verrata or OmniWire (Philips Healthcare, Amsterdam, NL). If the operator elected to proceed to PCI, a single target lesion was treated with a drug-eluting stent and optimized according to usual clinical practice. FFR and iFR were then both remeasured using the Verrata or OmniWire. After this, operators were free to further optimize the stented segment and/or treat the second serial lesion at their discretion.

***Pressure Wire Assessment***

Following administration of intracoronary nitrates, a pressure wire was calibrated to aortic pressure and advanced to the distal vessel with the pressure wire sensor ≥15 mm beyond the most distal stenosis, in a portion of the target vessel >2 mm diameter by visual estimation. The position was recorded using fluoroscopy and care was taken to record any subsequent measurements in the same location by reference to the stored fluoroscopy. Pd/Pa and whole vessel FFR/iFR was measured followed by a continuous manual pullback of the pressure wire sensor to the tip of the guiding catheter. Markers were placed to indicate the position of lesions for offline co-registration with the coronary anatomy. If there was drift >0.02 units, repeat pressure wire measurements were recommended. For FFR measurements, hyperemia was induced by intravenous administration of adenosine in all cases.

***Clinical Decision Making***

During the procedure the operator was asked to declare their treatment strategy at each stage, as incremental physiological data became available. This included their intended treatment modality (optimal medical therapy, PCI, or CABG) and, if this was PCI, the target lesion (proximal, distal, or both). Responses were documented using a dedicated questionnaire, which was administered after initial angiography, and on completion of the pre-PCI physiology assessment.

**Core Laboratory Analysis**

Quantitative coronary angiography (QCA) was performed using Medis QFR 2.2 Research Edition (Medis Medical Imaging, Leiden, NL). Physiology traces were assessed for technical quality and in those meeting minimum standards, the treated segments were co-registered on the pullback trace (Figure 1). This was by combination of coronary angiography, presence of abrupt increases in FFR/iFR (in focal disease), and site placed markers. Any pullbacks submitted with drift >0.02 and <0.05 were considered suitable for analysis and were algorithmically corrected.

The pressure pullback gradient (PPG) is an index ranging from 0 to 1 that characterizes the pattern of pressure loss within an artery, with 0 indicating diffuse disease and 1 indicating focal disease.8 This was automatically calculated from the pullback trace using Coroventis CoroFlow 3.5.1 (Abbott Laboratories, IL, USA).

***Prediction of post-PCI FFR/iFR***

Predicted post-PCI physiology after treatment of a single target lesion was calculated as follows (Supplementary figure S2): First, the FFR gradient across the treated segment was measured (dFFR) and added to the whole vessel FFR to estimate the post-PCI FFR (FFRΔ). The same process was applied to the iFR pullback to estimate post-PCI iFR (iFRΔ). FFRcalc, which accounts for the interaction between serial lesions during hyperemia, was calculated as previously described (Figure 1).12 In brief, this method assumes a linear relationship between trans-lesional pressure and flow, where the resistance of stenoses and the distal circulation remains fixed, regardless of the number of stenoses. This allows the post-PCI FFR to be calculated without the need for coronary occlusive pressure, which is impractical for routine clinical use.13

PPG has shown the ability to predict the final whole vessel FFR (Final FFRPPG) after PCI.8 We evaluated its performance against a δFFR based prediction in this dedicated cohort of serial coronary disease (Supplementary Appendix p4 and p5).

**Outcome Measures**

The primary outcome measure was the error between the predicted post-PCI FFR (FFRΔ) or iFR (iFRΔ), and the actual post-PCI FFR or iFR (Supplemental table S1). A significant residual gradient likely to be associated with ischemia was defined as a post-PCI FFR ≤0.80 or iFR ≤0.89. The clinically relevant misclassification rate was therefore defined as the proportion of cases where the pre-PCI prediction method incorrectly predicted a post-PCI FFR >0.80 or iFR >0.89. Secondary outcomes were a) the change in decision making following baseline physiological assessment, and after post-PCI physiological assessment and b) major adverse cardiovascular events (target vessel revascularization, myocardial infarction, stroke and all-cause death) at 1 year. As clinical follow-up is ongoing, we report here the primary and intra-procedural secondary outcomes.

**Statistical Analysis**

The statistical analysis plan is available in the supplementary appendix. Previous work has shown a 20% error in iFRD and 14% error in FFRcalc in predicting post PCI physiology.12 60 paired comparisons would be required to have 90% power to detect a difference in error rate of 6% between groups (at a significance level of 5%). Given that eligibility was based on angiographic criteria, we expected that a significant proportion of cases would not proceed to PCI (due to deferral based upon treatment thresholds, or physiologically diffuse disease that was unsuitable for PCI) and hence lack post-PCI physiology measurements. Accounting for a potential 50% loss after the initial physiological assessment, the target sample size was set at 120 patients. Recruitment was monitored by the trial steering committee with the intention to stop once 120 patients had been enrolled or 60 paired physiology datasets had been accrued, whichever occurred sooner.

Data are presented as mean ± SD or median and interquartile range according to distribution and compared with the Student’s *t*-test or Wilcoxon signed-rank test. Categorical variables are presented as number (percentage). The primary outcome was assessed using the Wilcoxon signed-rank test and continuous agreement between predicted and measured pressure-wire indices was compared using the Bland-Altman method. A pre-specified exploratory analysis was to identify the determinants of error in FFRcalc using Pearson’s correlation coefficients, univariate and multivariate regression. The secondary outcome was assessed using the McNemar-Bowker test. Applicable tests were two-tailed and a *P* value <0.05 was considered significant. All analyses were performed using R 4.4.1 (Foundation for Statistical Computing, Vienna, Austria).

## Results

**Baseline Characteristics**

Between September 2021 and July 2024, 87 participants were randomized with 45 assigned to FFR-guided treatment and 42 to iFR-guided treatment (Figure 2). Baseline characteristics were well matched and are shown in Table 1. The mean age was 67 ± 10 years, 28 (31%) were diabetic and 64 (74%) presented with stable angina. Baseline angiographic and physiological characteristics are shown in table 2.

Across the whole population, 72 patients (83%) were enrolled based upon the presence of two focal lesions. The target vessel was the left anterior descending artery (LAD) in 54 patients (64%) and the right coronary artery (RCA) in 28 patients (33%). The operator-identified target lesion was more severely stenosed (57 ± 14% vs. 46 ± 10%, p<0.0001), longer (29 mm [22 – 38] vs. 18 mm [15 – 26], p<0.0001) and with a larger reference diameter (2.87 ± 0.57 mm vs. 2.52 ± 0.47mm, p=0.0002), than compared to the second lesion in the target vessel. Of the 74 patients that proceeded to PCI, intracoronary imaging was used in 61 (82%) with the target lesion being reduced to ≤20% diameter stenosis in 71 (96%) patients (mean post-PCI diameter stenosis of 13 ± 9%). The mean trans-stent gradient within the FFR arm was 0.04 ± 0.03.

Drift leading to repeat pressure wire measurement was required for 27 of 264 (10%) pullbacks submitted to the core laboratory. Of the remaining 237 pullbacks, 33 (14%) showed drift >0.02 and <0.05 (the pre-specified range requiring offline algorithmic correction). The median baseline whole vessel pre-PCI FFR and iFR was 0.71 (0.64 to 0.80) and 0.82 (0.67 to 0.90), respectively. Baseline FFR and iFR discordance based upon binary thresholds of ≤0.80 for FFR and ≤0.89 for iFR was seen in 11 of 87 vessels (13%): 3 FFR-/iFR+ and 8 FFR+/iFR- (Supplementary figure S3).

**Performance of Predicted Indices**

Using the trans-lesional pullback gradient to predict the post-PCI FFR or iFR after treatment of a single target lesion, the median difference between FFRD and the actual post-PCI FFR was 0.10 (0.05 to 0.13) with 12% (5.7 to 17.2%) error. The median difference between iFRD and actual post-PCI iFR was 0.04 (0 to 0.08) with 4% error (0.0 to 9.0%, p<0.0001 versus FFRD). Using FFRcalc, the median difference was -0.05 (-0.15 to -0.06) with -5% (-18 to -8%, p=0.427 versus FFRD) error (Figure 3, Supplementary figures S4 and S5). When binary thresholds are applied, a significant post-PCI gradient was misclassified in 23 of 64 vessels (36%) with FFRΔ, 21 of 62 vessels (34%) with iFRΔ and 9 of 64 vessles (14%) with FFRcalc (p=0.002 for FFRcalc vs FFRΔ and p=0.008 for FFRcalc vs iFRΔ).

There was no significant difference in mean error for FFRcalc whether the target vessel was the LAD or RCA (-0.04 ± 0.15 versus -0.09 ± 0.18, p=0.43). Distal pressure was weakly correlated (*R*=0.38, 95% CI: 0.14 – 0.58) and the trans-lesional pressure gradient was strongly negatively correlated (*R*=-0.72, 95% CI: -0.82 – 0.57) with the FFRcalc error (Supplementary figure S6 and table S2).

**Management Strategy**

After declaring a management strategy based upon angiography alone, pre-PCI physiological assessment altered the treatment modality in 9 of 82 patients (11%). There was no difference between the FFR (4 of 43, 9%) and iFR (5 of 39, 13%) treatment arms (p=0.91). In the 67 cases where the operator proceeded to PCI, physiological assessment changed the target lesion in 11 patients (16%) with no difference between the FFR (5 of 37, 15%) and iFR 6 of 30, 20%) arms (p=0.70; Supplementary figures S7 and S8).

## Discussion

SERIAL is the first prospective, randomized, within-patient, head-to-head comparison of FFR versus iFR in serially diseased coronary arteries. First, we have found that in serial disease, performing coronary physiology with a pullback changes the target lesion in 1 in 6 cases. Second, that conventional use of the trans-lesional FFR or iFR gradient leads to overestimation of the post-PCI physiology result. Third, when binary treatment thresholds are applied, trans-lesional FFR or iFR based predictions will misclassify residual ischemia in over a third of cases (Central Illustration). Finally, whilst a calculation which accounts for the hemodynamic interaction between serial lesions is associated with a lower rate of misclassification, the spread of error is appreciable.

**Predicting Post-PCI Physiology**

Clinical coronary physiology has evolved from assessing hemodynamic significance at the vessel level, to longitudinally mapping pressure loss within a vessel by pullback of the pressure wire. Although hyperemia lends the FFR pullback a higher spatial resolution which is desirable in complex disease (as pressure loss is distributed over a wider range than iFR), there is a well-documented phenomenon of hemodynamic interaction between lesions, whereby a proximal lesion affects the distal lesion’s FFR and vice versa.13 Whilst it has previously been suggested that coronary autoregulation maintains constant flow at rest and therefore non-hyperemic indices such as iFR are less vulnerable to this interaction,10,14,15 systematic assessment across a range of serial stenoses has shown that iFR is not immune. Indeed, for more proximal and severe coronary disease, iFR (with its calculation exclusively in diastole) is paradoxically affected to a greater degree than Pd/Pa or FFR.16,17 In the current study, we observe that iFR performs no better than FFR in when using binary classification thresholds. The absolute error rate is greater than reported recently by Matsuo et al (0.036 ± 0.037)14 and markedly higher than earlier descriptions of the technique.9,15

Both FFRD and iFRD tend to overestimate the hemodynamic benefit of PCI to a single target lesion in serial and diffuse disease. This is consistent with previous work, although we found that FFRcalc underestimates the post-PCI FFR in contrast to the initial validation study.12 This may be explained by the inclusion of more severe and longer lesions in the present study. Whilst FFRcalc performs better than FFRΔ or iFRΔ on average, the larger spread of error suggests that this simple correction fails to account for the hemodynamic nuances that apply in more severe and complex disease.

Therefore, we advise caution when attempting to predict the physiological result after PCI in serial disease, particularly when the post-PCI result by FFRΔ or iFRΔ is predicted to be borderline. We would strongly recommend reassessment of physiology after target lesion PCI, with a view to further stent optimization or treatment of additional segments of vessel as required. In cases where further PCI would be either undesirable or not feasible, surgical revascularization or medical therapy should be considered from the outset..

**How common is serial disease?**

The angiographic or physiological definition of serial disease varies widely,11 with previous studies largely defining disease distribution and serial anatomy by a visual estimation of severity and lesion separation. In contrast, we pragmatically enrolled patients based upon the presence of a lesion that the operator judged to be suitable for treatment with a stent, with either a second lesion or a segment of diffuse disease. Furthermore, we report the treated segment length, which is invariably longer than the angiographic lesion length reported in other studies of serial disease.11 Given that even mild diffuse atheroma can cause pressure loss within a vessel18 and that truly normal coronary segments outside of the target segment are uncommon, the incidence of physiological serial disease is bound to be higher than reported in historical angiographic series. Recent efforts have been made to recognize that flow-limiting atheroma exists on a spectrum, and that we should be moving to a physiological classification, whereby relative focality is expressed using an objective continuous index, the PPG.8 Derived from the hyperemic pullback trace, the PPG has also been shown to predict the hemodynamic response to PCI. Although a model incorporating PPG (FFRPPG) was less accurate at predicting the final FFR in the present study compared to the initial validation cohort, it nonetheless performs better than a δFFR-based estimation (Supplementary appendix S9 and S10).

**Future Directions**

Functional coronary angiography (coronary physiology derived from angiography only) has proliferated in recent years, with ostensibly clear advantages in avoiding pressure wire use or the need for hyperemia, whilst offering implicit co-registration with angiography and reduced costs. Although multiple studies have suggested that functional coronary angiography indices are able to predict their own value post-PCI, or the FFR post-PCI, this has not yet been systematically tested in serially diseased arteries.19–22 With recent advances in ultra-high coronary CT angiography resolution, combined with its ability to generate a true 3-dimensional coronary model (as opposed to extrapolation from one or more views), it is possible that the effects of ‘virtual’ PCI may be best assessed from non-invasive data.23

**Limitations**

This study has some limitations. First, assessment of hyperemic physiology is imprecise without the automated co-registration of angiographic anatomy and physiology pullback traces, such as with iFR ScoutTM and SyncVision. This potential error is amplified with manual pullback where the pullback speed may be inconsistent, and in diffuse disease where clear physiological ‘plateaus’ may be absent. Nonetheless, most patients in this study were enrolled on the basis of 2 focal lesions. Second, pressure wire drift less than 0.02 was not corrected in this study. Whilst representative of real world clinical practice, in this population where the post-PCI indices lie close to binary cut-off values, small changes can significantly shift misclassification rates.24 Third, whilst all these techniques assume complete removal of the pressure gradient across a diseased segment, stent optimization techniques such as intracoronary imaging were not mandated (although this was performed as the standard of care in 82%). Conversely, the high use of intracoronary imaging optimized stents may dilute the impact of post-PCI physiology on clinical decisions.25 Fourth, this study was conducted in 4 experienced coronary physiology centers, but in wider practice it is only used in 20% of patients with intermediate lesions.24 Whist the use of a core laboratory ensures objective analysis, it is uncertain whether these results can be replicated in real-time, in a broader setting. Fifth, microcirculatory function and the degree of hyperemia present during post-PCI physiological assessment were not systematically quantified in this study. Finally, SERIAL was not powered to assess change in decision making, ischemia classification, or clinical outcomes.

## Conclusions

## Using pre-PCI FFR or iFR trans-lesional gradients to predict the physiological impact of PCI in serially diseased coronary arteries overestimates the benefit and often leads to the misclassification of residual ischemia. This can be improved using a technique that accounts for the hemodynamic interaction between stenoses but until validated in large studies, direct measurement of post-PCI physiology is strongly recommended.

## Clinical Perspectives

**What is Known?** Pre-PCI FFR or iFR pullbacks are commonly used to predict thephysiological effects of PCI, but this approach has not been systematically evaluated in serial and diffuse disease. **What is New?** Conventional use of pre-PCI FFR or iFR pullbacks systematically overestimates the benefit of PCI. Patients with a residual stenosis post-PCI should undergo repeat measurement of coronary physiology for definitive assessment of its hemodynamic significance. **What is Next?** Additional work is needed to understand the factors associated with error in the prediction of post-PCI physiology, with solutions to be tested in larger cohorts.

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## Figure Legends

**Figure 1. SERIAL Study Design & Example Case**

Two methods of predicting post-PCI physiology are tested in this study. First, by using the trans-lesional pressure gradient: δFFR and δiFR indicate the gradient in FFR/iFR units across the treated segment. This is added to the whole vessel FFR/iFR value to predict the FFR and iFR (FFRΔ orFFRΔ) after PCI to the target lesion. Second, by using a method that aims to account for the hemodynamic interaction between serial lesions: FFRcalc uses absolute pressure values in mmHg, dP indicates the gradient across the treated segment and Pd indicates distal pressure measured at the beginning of the pullback trace. In this example, the patient has been randomized to FFR-guided treatment. Both FFR and iFR pullbacks are performed pre- and post-PCI, however the operator is blinded to the iFR results throughout.

**Figure 2. Study Flow Chart**

FFR: fractional flow reserve; iFR: instantaneous wave free ratio.

**Figure 3**. **Difference Between Predicted and Actual FFR/iFR**

Comparison of FFRΔ, iFRΔ, FFRcalc and the actual measured indices for the 59 participants with paired FFR and iFR measurements made pre- and post-PCI. A positive value indicates overestimation, and a negative value indicates underestimation of the post-PCI FFR/iFR.

**Central Illustration. FFR versus iFR in Serial and Diffuse Disease**

The SERIAL study was a randomized, within patient comparison of FFR and iFR in serial and diffuse coronary disease. It evaluated the ability of the pre-PCI FFR or iFR pullback to predict the physiology after treatment of a single target lesion.

## Tables

**Table 1. Baseline Demographics**

|  |  |  |
| --- | --- | --- |
|  | **FFR-guided**  **(n=45)** | **iFR-guided**  **(n=42)** |
| **Demographics**  Age  Male  BMI | 67 ± 11  34 (76)  27.7 ± 4.8 | 69 ± 10  34 (81)  28.5 ± 5.4 |
| **Past Medical History**  Diabetes  Hypertension  Hypercholesterolaemia  Current smoking  Chronic kidney disease (eGFR <60)  Peripheral vascular disease  Previous MI  Previous PCI | 12 (27)  25 (58)  21 (50)  11 (31)  6 (15)  2 (5)  13 (30)  15 (36) | 15 (36)  23 (56)  24 (63)  6 (18)  6 (16)  1 (3)  19 (46)  22 (52) |
| **Presentation**  Stable angina  Unstable angina  NSTEMI/staged STEMI  LVEF | 33 (77)  5 (12)  5 (12)  54 ± 8% | 31 (78)  4 (10)  5 (13)  53 ± 8% |
| **Symptoms**  CCS angina class  1-2  3-4  NYHA  I-II  III-IV | 23 (64)  13 (36)  27 (84)  5 (16) | 18 (62)  11 (38)  21 (78)  6 (22) |

BMI: body mass index; CCS: Canadian Cardiovascular Society; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NSTEMI: non-ST elevation myocardial infarction; NYHA: New York Heart Failure Association; STEMI: ST-elevation myocardial infarction. Data are presented as counts (percentage) and mean ± SD. Percentages may not total 100% due to missing data.

**Table 2. Baseline Angiographic and Physiological Characteristics**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All (n=87)** | **FFR arm (n=45)** | **iFR arm (n=42)** |
| **Target vessel**  LAD  LCx  RCA | 54 (64)  3 (4)  28 (33) | 28 (64)  3 (7)  13 (30) | 26(63)  0 (0)  15 (37) |
| **Abbott pressure wire**  Pd/Pa  FFR  PPG | 0.87 (0.80 – 0.93)  0.70 (0.62 – 0.78)  0.59 (0.51 – 0.72) | 0.86 (0.76 – 0.91)  0.70 (0.55 – 0.75)  0.60 (0.50 – 0.73) | 0.88 (0.83 – 0.95)  0.72 (0.65 – 0.83)  0.58 (0.53 – 0.72) |
| **Phillips pressure wire**  Pd/Pa  iFR | 0.86 (0.77 – 0.92)  0.82 (0.67 – 0.90) | 0.86 (0.76 – 0.90)  0.78 (0.67 – 0.86) | 0.88 (0.80 – 0.93)  0.84 (0.70 – 0.92) |
| **Pre-PCI QCA**  Lesion 1 diameter stenosis  Lesion 1 length  Lesion 1 RVD  Lesion 2 diameter stenosis  Lesion 2 length  Lesion 2 RVD | 57 ± 14  29 (22 – 38)  2.87 ± 0.57  46 ± 10  18 (15 – 26)  2.52 ± 0.47 | 60 ± 14  29 (20 – 38)  2.79 ± 0.57  47 ± 10  19 (15 – 26)  2.48 ± 0.42 | 53 ± 12  30 (24 – 37)  2.97 ± 0.56  46 ± 11  17 (15 – 23)  2.58 ± 0.53 |
| **Post-PCI QCA**  Lesion 1 diameter stenosis | 13 ± 9 | 13 ± 11 | 14 ± 6 |
| **Pullback Analysis**  dFFR  diFR  dpressure (mmHg)  Distal pressure (mmHg) | 0.18 (0.12 – 0.27)  0.12 (0.06 – 0.23)  17 (10 – 23)  54 (45 – 62) | 0.21 (0.12 – 0.30)  0.14 (0.07 – 0.23)  19 (12 – 24)  42 (44 – 55) | 0.17 (0.13 – 0.22)  0.11 (0.07 – 0.23)  17 (10 – 23)  58 (50 – 64) |
| **Predicted Post-PCI Physiology**  FFRD  iFRD  FFRcalc | 0.90 (0.85 – 0.93)  0.93 (0.90 – 0.96)  0.76 (0.68 – 0.85) | 0.90 (0.84 – 0.94)  0.93 (0.91 – 0.96)  0.73 (0.59 – 0.84) | 0.91 (0.86 – 0.93)  0.94 (0.90 – 0.97) 0.79 (0.71 – 0.85) |
| **Actual Post-PCI Physiology**  FFR  iFR | 0.82 (0.74 – 0.87)  0.89 (0.83 – 0.93) | 0.79 (0.70 – 0.87)  0.89 (0.82 – 0.94) | 0.83 (0.75 – 0.88)  0.88 (0.84 – 0.92) |

Lesion 1 refers to the operator determined target lesion for PCI. Post-PCI physiology refers to the predicted values after treatment of this single target lesion only. Comparisons between treatment arms for Pd/Pa (Abbott) p=0.037, Distal pressure p=0.044, baseline iFR p=0.043, lesion 1 diameter stenosis p=0.035. All other comparisons non-significant.

LAD: Left anterior descending artery; LCx: Left circumflex artery; RCA: Right coronary artery; FFR: Fractional flow reserve; RVD: reference vessel diameter. Data are presented as counts (percentage), mean ± SD for normally distributed and median (IQR) for non-normally distributed data.