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ORIGINAL ARTICLE

Segmental post-percutaneous coronary intervention physiological gradients using ultrasonic or optical flow ratio: insights from ASET JAPAN study

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Abstract

Aims

Segmental pressure gradients post-percutaneous coronary intervention (PCI) can detect residual disease and optimization targets. Ultrasonic flow ratio (UFR) or optical flow ratio (OFR) offer simultaneous physiological and morphological assessment using a single imaging catheter. This study evaluated the utility of UFR and OFR in identifying residual disease post-PCI.

Methods and results

The study include patients from the Acetyl Salicylic Elimination Trial JAPAN Pilot study with complete intravascular imaging pullback data, where UFR or OFR was obtained post-PCI. Anatomical focal lesions distal and proximal to the stent were analysed in segments ≥5 mm long. UFR or OFR virtual pullback curves assessed intra-stent pressure gradients, defining physiological focal or diffuse by segmental pressure drops ≥0.05 over lengths <10 or ≥10 mm, respectively. The median post-PCI UFR/OFR was 0.93 (0.88–0.96) with 35.4% (69/195) vessels having a UFR/OFR < 0.91. There were significantly more focal lesions, both anatomical and physiological, proximal and distal to the stent in vessels with UFR/OFR < 0.91 compared with those ≥0.91. Agreement between anatomical and physiological focal lesions was moderate proximally (kappa = 0.553, $P < 0.001$) and fair distally (kappa = 0.219, $P = 0.002$). The in-stent gradient poorly predicted significant stent under-expansion. However, the virtual fractional flow reserve gradient performed well in detecting proximal or distal focal disease (area under the curve = 0.835 and 0.877, respectively).

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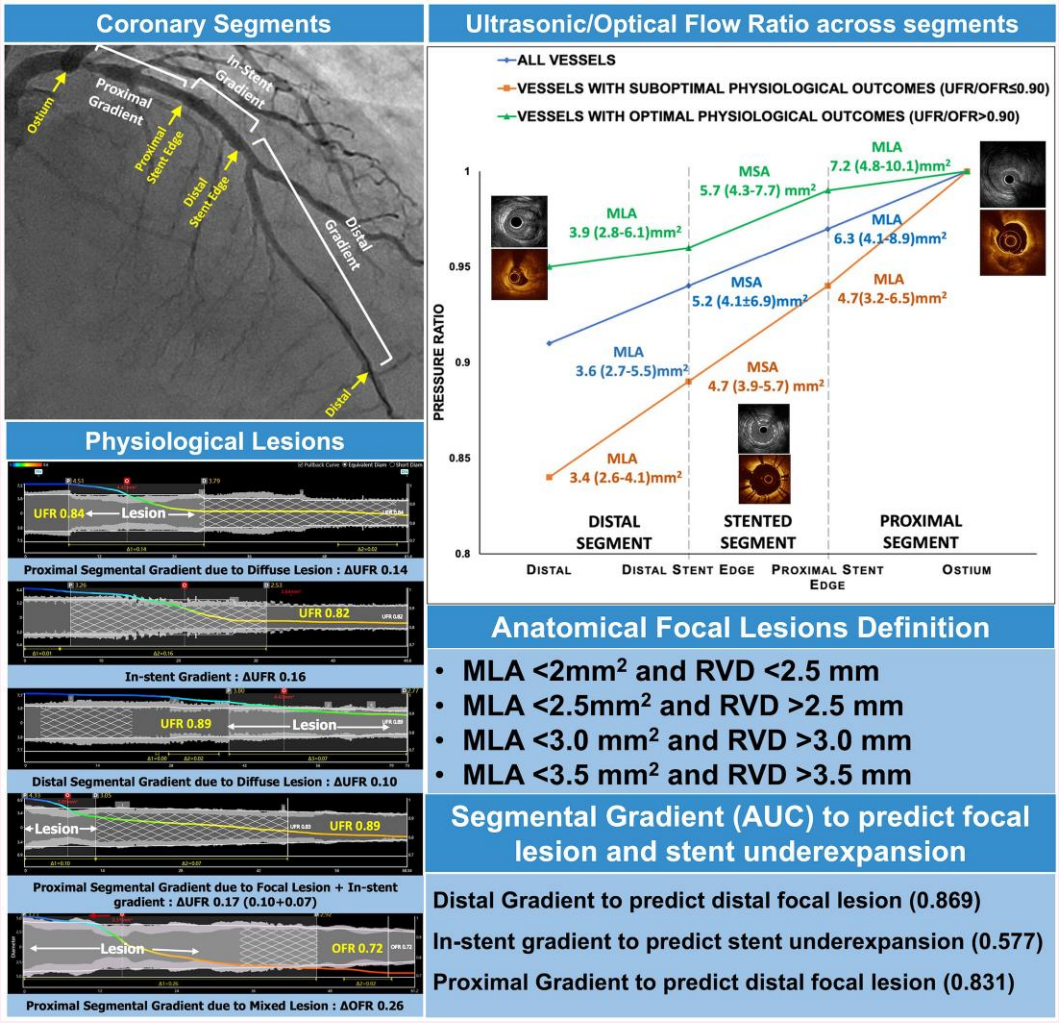
Conclusion UFR/OFR effectively identifies sub-optimal vessel physiology post-PCI and locates precise anatomical issues, validated by intravascular imaging.

Trial registration The ASET JAPAN ClinicalTrials.gov reference: NCT05117866

Graphical Abstract



Segmental Virtual FFR Gradients Post-PCI and Intravascular Imaging Detected Residual Lesions and Stent Under-expansion.

A total of 195 vessels with post-percutaneous coronary intervention (PCI) underwent intravascular imaging (IVUS or OCT). Virtual FFR gradients were calculated based on the ultrasonic flow ratio or optical flow ratio pull back curve in the Acetyl Salicylic Elimination Trial (ASET) JAPAN Pilot study Phase I. Virtual pressure ratios were calculated at four locations: distal, the distal and proximal stent edges, and the coronary ostium. Segmental pressure gradients were defined as the difference between the proximal and the distal pressure ratio value. Lesions (focal, diffuse, and mixed) were classified as physiological in segment lengths ≥10 mm and anatomical (focal) lesions in segment lengths ≥5 mm. The performance of segmental virtual FFR gradients was good to detect anatomical focal lesions. There was moderate agreement between proximal anatomical focal and physiological focal lesions. Minimal lumen area [median (IQ)] and minimum stent area [median (IQ)] are indicated in different colours (green, blue, and orange) in corresponding coronary segments.

Keywords virtual FFR gradient derived from IVUS or OCT • ultrasonic flow ratio • optical flow ratio

Introduction

Revascularization guidelines recommend using fractional flow reserve (FFR) or non-hyperemic pressure ratios (NHPRs) prior to considering percutaneous coronary intervention (PCI) of intermediate coronary artery lesions.[1,2] Notably, whilst angiographically successful PCI re-establishes epicardial conductance and improves myocardial perfusion, in a sizable proportion of patients epicardial haemodynamics remain abnormal.[3] As such, sub-optimal post-PCI physiology and focal residual disease, as detected by intravascular imaging, occurs in up to 60% of cases and has been directly linked to future events.[4–8] At present, uncertainty exists on how residual disease should be detected, and whether potential optimization treatment should be guided by FFR or intravascular imaging,[9] with the latter identifying major causes of target-vessel failure (TVF) like stent under-expansion, residual (non-obstructive) disease at stent edges, irregular tissue protrusion, stent edge dissection, and major strut malapposition.[10]

Ultrasonic flow ratio (UFR) and optical flow ratio (OFR) are novel validated methods for the rapid computation of FFR, which are derived from intravascular ultrasound (IVUS) or optical coherence tomography (OCT) images and combine plaque morphology and coronary physiology thereby obviating the need for two diagnostic procedures and two separate intravascular instrumentations. Notably, previous studies have extensively validated UFR/OFR against wire-based FFR, in both pre- and post-PCI settings supporting its utility as a reliable surrogate for physiological assessment.[11–17]

Given the potential benefits in combining the physiological and morphological assessment of lesions, this study aimed to evaluate for the first time the utility of using UFR and OFR to identify residual disease post-PCI in segments of stented and non-stented coronary arteries.

Methods

The present study is a sub-analysis of the ASET JAPAN pilot study Phase I. The design, patient inclusion and exclusion criteria, and main results have already been published.[18,19] In short, the study showed the feasibility and safety of low dose prasugrel monotherapy following PCI in Japanese patients presenting with chronic coronary syndrome (CCS) and an anatomical SYNTAX score <23.[19] The certified review board, Central Ethics Committee and Local Ethics Committee at each participating centre approved the study protocol (Reference no. CRB4180003). All enrolled patients provided written informed consent, and the study complied with the Declaration of Helsinki.

Procedure

All patients received SYNERGY (Boston Scientific, Natick, USA) drug eluting stents; IVUS or OCT whilst not mandatory was performed in 99.6% of cases according to local practice. Post-procedure, an IVUS or OCT pull back was performed starting from at least 5 mm distal to the stent edge or from a distal anatomical landmark.

Quantitative and qualitative assessment of IVUS or OCT pullbacks was performed by automatically delineating vessel, lumen, and stent contours every 0.5 mm using QCU-CMS (version 4.69, Division of Image Processing, Leiden University Medical Centre).

UFR or OFR was calculated using the respective IvusPlus or OctPlus software, Pulse Medical, Shanghai, China.[11,14] All UFR and OFR tracings, and IVUS and OCT pullbacks were analysed at the CORRIB Core Lab, Galway, Ireland by two analysts blinded to clinical and procedural data. The time required to calculate OFR or UFR for 10 random vessels was 60 ± 25 and 98 ± 22 s, respectively.

Segmental pressure gradients were derived from UFR or OFR virtual pull back curves in segments ≥5 mm long and defined as: (i) the distal pressure gradient: difference in virtual pressure between the most distal UFR or OFR measurement and the distal stent edge; (ii) the in-stent gradient was the pressure difference between the distal and proximal stent edge; and (iii) the proximal gradient was the difference between the proximal stent edge and the coronary ostium (left anterior descending (LAD)/RCA ostium). ('*Graphical Abstract*') When the ostium of the LAD had a plaque burden of >40% the analysis was performed from the left main ostium.

The present sub-analysis focused on the following qualitative and quantitative findings:

(1) Physiological assessment of focal, mixed, and diffuse lesions distal and proximal to the stent. Physiologically, residual lesions were defined as (i) focal if the UFR or OFR dropped by ≥0.05 over a distance of <10 mm (ΔUFR or ΔOFR ≥ 0.05 in <10 mm), (ii) diffuse if there was a progressive decline in the UFR or OFR of ≥0.05 over a distance ≥10 mm, and (iii) mixed lesions if there was a combination of focal and diffuse lesions ('*Graphical Abstract*').[20,21]

(2) Anatomical assessment of focal lesions, distal and proximal to the stent. Anatomically, residual focal lesions were defined as follows: (i) lesion with minimal lumen area (MLA) < 2 mm^2 and reference vessel diameter (RVD) < 2.5 mm^2; (ii) lesion with MLA < 2.5 mm^2 and RVD > 2.5 mm; (iii) lesion MLA < 3.0 mm^2 and RVD > 3.0 mm; (iv) lesion MLA < 3.5 mm^2 and RVD > 3.5 mm.[22–24]

(3) Correlation between stent under-expansion, as assessed by QCU-CMS software, and in-stent virtual pressure gradient, as assessed by the UFR or OFR virtual pullback curve. In-stent gradient was defined as a pressure drop within the stent derived from the UFR or OFR virtual pullback curve. Stent expansion index (SEI) was evaluated as the minimum stent area (MSA)/average of proximal and distal reference lumen area × 100.[25] An SEI ≤ 80% was considered as stent under-expansion. The proximal and distal reference segments were measured at normal-looking cross-sections within 5 mm proximal or distal to the stent.

Detailed methodology for post-PCI UFR and OFR analysis is provided in the Supplementary data online, Supplement material. The correlation and agreement between wire FFR and UFR/OFR in a subset of vessels ($n = 16$) before PCI is provided in the supplement (see Supplementary data online, *Figure S1*).

Whilst this study could not evaluate the correlation and agreement between UFR and OFR due to the absence of both IVUS and OCT on the same vessel segment, we analysed data from 39 segments where both modalities were used in a different population to identify vulnerable plaques. Independent blinded analysts at the Core Lab conducted the analysis (see Supplementary data online, Supplement material). The correlation between UFR and OFR was excellent, with a coefficient of $r = 0.84$ (see Supplementary data online, *Figure S2*).

Statistical analysis

All continuous variables under investigation showed a non-normal distribution (according to the Shapiro–Wilk test) and are reported as median (IQR). Categorical data are reported as number and proportion. The correlation between continuous variables was evaluated using the Spearman correlation coefficient. Differences in segmental pressure gradients between vessels with and without sub-optimal physiological outcomes and between vessels with and without IVUS-defined residual disease were evaluated using the Mann–Whitney *U* test. Receiver-operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of the segmental pressure gradients to detect residual focal disease identified by IVUS/OCT imaging abnormalities. ROC curves were compared using the DeLong's test. Analyses also included evaluation of diagnostic performance of segmental gradients normalized for segment length (segmental gradient/segment length × 10). The weighted kappa statistic was employed to evaluate the agreement between focal anatomical and physiological lesions. All statistical analyses were performed using IBM SPSS Statistics for Windows (version 24.0) and R (version 3.5.2, package: proc, R Foundation for Statistical Computing).

Results

A total of 188 patients with 195 treated vessels had complete IVUS (138 vessels and 138 IVUS pullbacks) or OCT (57 vessels and 57 OCT pullbacks) pullback data. Patient and vessel characteristics are presented in *Tables 1* and *2*, respectively. Mean age was 68.86 ± 9.79 years,

154 (82%) patients were male, and 34% had diabetes. The LAD was the vessel of interest in 66.2% of cases, followed by the RCA (16.4%); 42% of lesions were type B2 or C (*Table 1*). The median virtual FFR derived from UFR or OFR pullback curves was 0.93 (IQ 0.88–0.96) ('*Graphical Abstract*').

In the overall population, the median post-PCI minimal lumen areas (MLAs) distal and proximal to the stent were 3.62 (IQ 2.68–5.467) mm^2 and 6.25 (IQ 4.07–8.96) mm^2, respectively; the median MSA was 5.24 (IQ 4.11–6.90) mm^2. Residual anatomical and physiological disease is tabulated in *Table 2*. Stent under-expansion (SEI ≤ 80) was present in 82 (42.1%) vessels. Virtual segmental FFR gradients were larger in vessels with vs. without residual anatomical focal lesions (*Figure 1A*). The in-stent virtual FFR gradient was similar between vessels with and without stent under-expansion (0.042 ± 0.033 vs. 0.035 ± 0.033, $P = 0.202$, *Figure 1A*); however, it was significantly higher in vessels with under-expansion when adjusted for segment length (0.015 ± 0.011 vs. 0.011 ± 0.009, $P = 0.014$). Correlations between segmental gradients, MLA and segment length, and correlations between stent gradient, MSA, SEI, and stent length are summarized in *Table 3*.

Vessels with sub-optimal physiological outcomes

A total of 69 of the 195 vessels had a UFR or OFR ≤ 0.90. The median virtual FFR derived from IVUS or OCT of vessels with sub-optimal vs. optimal physiology was 0.86 (0.825–0.89) and 0.94 (0.95–0.97), respectively ($P < 0.001$). The anatomical and physiological characteristics of all treated vessels stratified according to a UFR/OFR ≤ 0.90 or >0.90 is shown in *Table 4*.

Vessels with residual anatomical focal lesions had larger segmental virtual FFR gradients compared with those without (*Figure 1B*). The in-stent virtual FFR gradient between vessels with and without stent under-expansion was not significantly different (0.07 ± 0.04 vs. 0.06 ± 0.04, $P = 0.843$, *Figure 1B*), even after adjustment for segment length (0.02 ± 0.01 vs. 0.02 ± 0.01, $P = 0.257$).

Correlations between segmental gradients, MLA and segment length, and correlations between stent gradient, MSA, SEI, and stent length are summarized in Supplementary data online, *Table S1*.

Table 1 Baseline characteristics of the patients in the study

	Patients ($n = 188$)
Age (years)	68.86(9.79)
Male (%)	154/188 (82%)
Female (%)	34/188 (18%)
BMI (kg/m^2)	24.75(3.94)
Smoking (%)	33/188 (17.6%)
DM (%)	64/188 (34%)
Hypertension (%)	150/188 (79.8%)
Hyperlipidaemia (%)	156/188 (83%)
Family history of CAD	10/188 (5.3%)
Previous MI	24/188 (12.8%)
Previous PCI	45/188 (24%)
Previous CABG	3/188 (1.6%)
Established peripheral vascular disease	11/188 (5.8%)
Chronic obstructive pulmonary disease	9/188 (4.8%)
Renal insufficiency (%) (eGFR < 60 mL/min/1.73 m^2)	68/188 (36.2%)
LVEF (%) ($n = 155$)	60.5 (10.1)
Anatomical SYNTAX score	8.2 (4.7)
AHA Lesion Type ($n = 195$)	
A	48/195 (24.6%)
B1	66/195 (33.8%)
B2	49/195 (25.1%)
C	32/195 (16.4%)

AHA, American Heart Association; BMI, body mass index (kg/m^2); DM, diabetes mellitus; CABG, coronary artery bypass grafting; CAD, coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; SYNTAX, synergy between percutaneous coronary intervention with Taxus and cardiac surgery

Table 2 Characteristics of vessels with intravascular imaging (IVI) (IVUS or OCT) ($n = 195$)

IVUS pull backs	138 (195) 70.8%
OCT pull backs	57 (195) 29.2%
UFR or OFR value median (quartiles)	0.93 (0.88–0.96)
Target vessel with IVI (*n*, %)	
Left anterior descending artery	129/195 (66.2%)
Left circumflex artery (including Ramus intermedius)	31/195 (15.9%)
Right coronary artery	32/195 (16.4%)
Diagonal	3/195 (1.5%)
Stent diameter, mm (195/195) median (quartiles)	3 (2.75–3.50)
Total stent length, mm (195/195) median (quartiles)	24 (20–32)
IVUS/OCT and UFR/OFR findings available	195/195 (100%)
Distal segment length ≥5 mm	182/195 (93.33%)
Distal segment length ≥10 mm	147/195 (75.38%)
Identification of distal focal lesion in these segments	
Anatomical	16/182 (8.8%)
Physiological	3/147 (2.04%)
Distal MLA, mm^2 (192/195) median (quartiles)	3.62 (2.68–5.48)
Distal segment length, mm (192/195) median (quartiles)	11.5 (10–16.52)
Distal UFR/OFR gradient, (192/195) median (quartiles)	0.015 (0.010–0.030)
Distal UFR/OFR gradient normalized for segment length, (192/195) median (quartiles)	0.012 (0.005–0.020)
In-stent segment	195/195
MSA, mm^2 (195/195) median(quartiles)	5.24 (4.11–6.90)
Stent expansion index (SEI) (195/195) %; mean (SD)	831 (7.4) %
Stent expansion	
SEI ≤ 80	82/195 (42.1%)
SEI > 80%	113/195 (57.9%)
In-stent segment length, in mm (195/195) median (quartiles)	26.8 (20.6–34.2)
In-stent UFR/OFR gradient (195/195) median (quartiles)	0.030 (0.010–0.050)

Continued

Table 2 ***Continued***

In-stent UFR/OFR gradient normalized for stent length (195/195) median (quartiles)	0.011 (0.005–0.018)
Proximal segment length ≥5 mm	161/195 (82.6%)
Proximal segment length ≥10 mm	148/195 (75.9%)
Identification of proximal focal lesion in these segments	
Anatomical	26/161 (13.3%)
Physiological	14/148 (9.5%)
Proximal MLA, mm^2 (185/195) median (quartiles)	6.25 (4.07–8.96)
Proximal segment length, mm (185/195) median (quartiles)	13.40 (10–24.10)
Proximal UFR/OFR gradient (185/195) median (quartiles)	0.020 (0.010–0.040)
Proximal UFR/OFR gradient normalized for segment length (185/195) median (quartiles)	0.013 (0.004–0.024)
Distal physiological focal lesion	2/147, 1.4%
Distal physiological mixed lesion	1/147, 0.7%
Distal physiological diffuse lesion	14/147, 9.5%
Proximal physiological focal lesion	9/148, 6.1%
Proximal physiological mixed lesion	5/148, 3.4%
Proximal physiological diffuse lesion	22/148, 14.9%

IVUS, intravascular ultrasound; OCT, optical coherence tomography; OFR, optical flow ratio; UFR, ultrasonic flow ratio; SEI, stent expansion index; MLA, minimal lumen area.

Diagnostic performance of post-PCI segmental gradients

In-stent virtual FFR gradient had poor discriminative ability to detect significant stent under-expansion (*Figure 2*), which remain unchanged even when corrected for segment length (area under the curve (AUC): 0.577 vs. 0.595, $P = 0.45$). The diagnostic performance remained poor, irrespective of vessel location (see Supplementary data online, *Table S2*).

Overall, the performance of a proximal virtual FFR gradient to detect proximal anatomical focal disease, and a distal virtual FFR gradient to detect distal anatomical focal disease was good and not significantly different (AUC: 0.877 vs. 0.835, $P = 0.43$, respectively) (*Figure 2*). The performance of a proximal and distal virtual FFR gradient to detect focal lesion adjusted for segment length is summarized in Supplementary data online, *Table S2*.

In the LAD, the performance of a proximal virtual FFR gradient to detect a proximal anatomical focal lesion, and a distal virtual FFR gradient to detect a distal anatomical focal lesion was good and not significantly different (AUC: 0.869 vs. 0.831, $P = 0.64$, respectively) (*Figure 3A*) (see Supplementary data online, *Table S2*). In non-LAD vessels, the performance of a distal virtual FFR gradient to detect a distal anatomical focal lesion was high (AUC: 0.964), whilst a proximal virtual FFR gradient to detect a proximal anatomical focal lesion was good (AUC: 0.820) and differed significantly ($P = 0.02$) (*Figure 3B*). Overall, the performance of proximal MLA to detect proximal focal physiological lesions ($n = 13$ lesions) was good (AUC—0.884; Youden index—4 mm^2), whilst the performance of distal MLA to detect distal focal physiological lesions was poor ($n = 3$ lesions) (AUC—0.378; Youden index—3.5 mm^2).

The diagnostic performance of segmental virtual FFR gradients to detect focal lesions and stent gradients to detect stent under-expansion in vessels with global sub-optimal physiological outcomes and stratified by

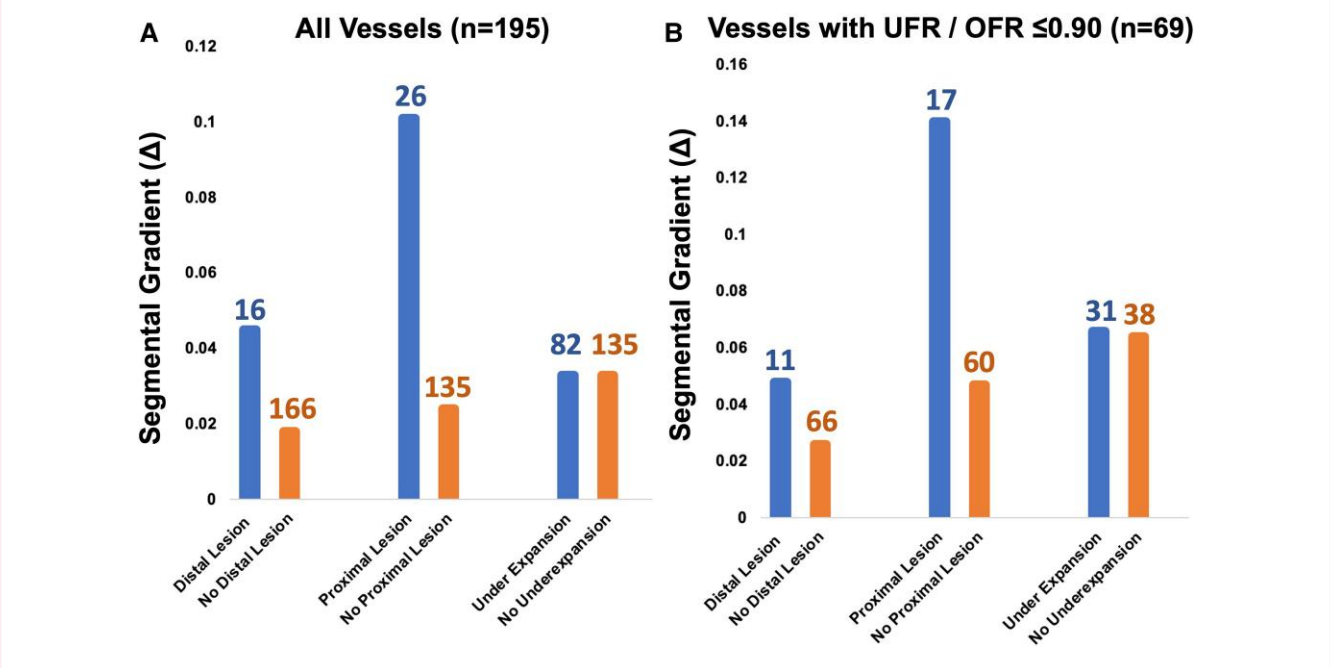


Figure 1 Segmental physiological gradients in vessels with and without IVUS-detected anatomical focal disease and vessels with and without stent under-expansion. (*A*) All vessels ($n = 195$); (*B*) vessels with UFR/OFR ≤ 0.90. Virtual segmental FFR gradients were larger in vessels with residual anatomical focal lesions when compared with vessels without focal lesions. Number on the top of each bar graph represents number of vessels. UFR, ultrasonic flow ratio; OFR, optical flow ratio.

Table 3 Correlation between segmental gradients, MLA and segment length, and correlation between stent gradient, MSA, SEI and stent length

Correlated variables	Spearman's correlation co-efficient (ρ)
Distal gradient and distal segment length	0.533(0.420–0.630), $P < 0.001$
Stent gradient and stented segment length	0.493(0.375–0.595), $P < 0.001$
Proximal gradient and proximal segment length	0.629(0.530–0.711), $P < 0.001$
MSA and stent gradient	−0.176(−0.313 to −0.032), $P = 0.014$
Stent gradient and stent expansion index	−0.195(−0.331 to −0.052), $P = 0.006$
Distal gradient and distal MLA	−0.381(−0.499 to −0.249), $P = 0.014$
Proximal gradient and proximal MLA	−0.591(−0.680 to −0.485), $P < 0.001$

MLA, minimal lumen area; MSA, minimum stent area; SEI, stent expansion index.

LAD and non-LAD is summarized in Supplementary data online, *Table S2*.

Overall (195 vessels), there was only slight agreement between distal anatomical focal and distal physiological focal lesions ($\kappa = 0.182$), whilst there was moderate agreement between proximal anatomical focal and proximal physiological focal lesions ($\kappa = 0.429$) (see Supplementary data online, *Table S3*).

In vessels with sub-optimal physiological outcomes ($n = 69$), there was fair agreement between distal anatomical focal and distal physiological focal lesions ($\kappa = 0.219$), whilst there was moderate agreement between proximal anatomical focal and proximal physiological focal lesions ($\kappa = 0.553$) (see Supplementary data online, *Table S3*).

At 1-year follow-up patient-oriented clinical endpoints [POCE—composite of all-cause mortality, any stroke, any myocardial infarction (MI) including non-target-vessel territory, and any revascularization] did not differ between patients with optimal and sub-optimal UFR/OFR (7.5 vs. 7.2%, Log-Rank $P = 0.96$) (*Figure 4*). The POCE was mainly driven by non-target vessel revascularization. Relationship between a low post-PCI UFR/OFR (<0.91) and 1 year all-cause mortality, any MI and any revascularization is provided in Supplement (see Supplementary data online, *Figures S3–S5*).

Discussion

The present study is a comprehensive intravascular imaging and virtual pressure gradient analysis to detect local anatomical and physiological abnormalities post-PCI. We conclude that: (i) segmental post-PCI virtual FFR gradients have a good ability to predict IVUS or OCT defined anatomical focal lesions, (ii) segmental virtual FFR gradients (distal, stent, and proximal) are more frequent in patients with a UFR/OFR ≤ 0.90, (iii) virtual in-stent pressure gradients are not able to distinguish between well-expanded and under-expanded stents, (iv) patients with a UFR/OFR ≤ 0.90 have more residual lesions (both anatomical focal and physiological) post-PCI, and a lower MSA, (v) residual anatomical focal lesions had fair to moderate agreement with residual physiological focal lesions, (vi) virtual segmental pressure gradients have moderate to strong correlation with the segment length.

In patients with CCS revascularization guidelines recommend FFR or NHPR to guide PCI of angiographically intermediate stenoses (Class IA).[26–29] Intracoronary imaging using IVUS or OCT has also now emerged as an important modality for lesion assessment and optimizing outcomes from PCI,[28,29] with several randomized studies showing that using it to guide complex PCI results in decreased rates of MACE compared with angiography alone.[30,31] The latest European Society of Cardiology (ESC) Guidelines provide a Class IA recommendation for intracoronary imaging guidance using IVUS or OCT during PCI for anatomically complex lesions, including left main stem, true bifurcations, and long lesions in patients with CCS.

The high incidence of sub-optimal physiology immediately after PCI mandates an investigation into the potential underlying mechanisms. Multiple factors, alone or in combination, are commonly involved, with the most frequent cause untreated stenoses, including diffuse, non-significant narrowing beyond the stent. The Fractional Flow Reserve Stent Evaluated at Rotterdam Cardiology Hospital (FFR-SEARCH) study documented a significant pressure drop (FFR drop >0.05) in 18% of stented segments, with proximal and distal coronary vessel segment involvement in 15 and 32%, respectively. In the multi-centre prospective HAWKEYE study, angiography based computational FFR (QFR) identified that in vessels with sub-optimal post-PCI QFRs (≤0.89), the residual pressure drop was located inside the stent in 13% of cases and outside the stent in 87%.[32]

Post-PCI FFR has been proposed as a clinical target to optimize PCI and as a surrogate endpoint for clinical outcomes.[4,33]

TVF can arise from stent-related problems or the presence and/or progression of disease in untreated segments.[34,35] Data suggest that a significant amount of residual disease remains unrecognized by post-PCI angiography.[3,4,8] In the present study, we aimed to elucidate the relationship between residual anatomical focal disease, and residual physiologically focal and diffuse disease as detected by IVUS or OCT, and segmental virtual FFR gradients. The largest virtual FFR drops were observed proximal to the stent, contrary to prior studies where the largest drops were distal,[22] a finding possibly due to the distal analysed segment being shorter than the proximal one in our study. In vessels with global sub-optimal post-PCI physiology, focal residual disease as detected by intravascular imaging techniques occurs in up to 60% of cases and has been directly linked to future events.[4–8,36]

To the best of our knowledge, no studies have been performed to evaluate the appropriateness of a segmental virtual pressure gradient to detect residual physiologically focal, mixed, or diffuse lesions distal or proximal to the stent, as assessed by intravascular imaging-based physiology. In fact, two dedicated PCI optimization trials designed optimization protocols that promoted additional stenting based on a focal FFR [Trial of Angiography vs. pressure-Ratio-Guided Enhancement Techniques-Fractional Flow Reserve (TARGET FFR)] or NHPR pressure gradient (DEFINE GPS; NCT04451044) (Distal Evaluation of Functional Performance With Intravascular Sensors to Assess the Narrowing Effect: Guided Physiologic Stenting).[33] In the present study we found that the distal and proximal segmental gradient showed good ability to identify residual corresponding anatomically focal lesions.

Several studies have reported on the relation between distal post-PCI FFR values and stent expansion.[37–40] In the present study, we found that UFR/OFR did not have any discriminative ability to detect stent under-expansion similar to the findings of FFR-SEARCH IVUS sub-study, in which no statistically significant differences were observed in 107 vessels between in-stent FFR gradients and the percentage of stent under-expansion, which ranged from 10 to 50%.[8] Similar to our study, in a sub-study of FFR REACT involving 132 patients (139 vessels) there was no significant difference in the in-stent FFR gradient between vessels with and without stent under-expansion.[22,41] We found an inverse correlation between MLA, MSA, and segmental gradients even when adjusted for segment length, which is consistent with previous studies showing inverse correlation between MLA and FFR.[23] Furthermore our findings that stent and segmental lengths (as assessed by IVUS or OCT) directly correlated with stent and segmental

Table 4 Vessel characteristics among patients with and without global sub-optimal physiological outcomes (UFR or OFR ≤ 0.90)

	UFR or OFR >0.90 ($n = 126$)	UFR or OFR ≤0.90 ($n = 69$)	*P*-value
IVUS	88/126 (69.84%)	50/69 (72.46%)	
OCT	38/126 (30.16%)	19/69 (27.54%)	
UFR/OFR, 195/195 median (IQ)	0.95 (0.94–0.97)	0.86 (0.825–0.89)	<0.001
Target vessel			
Left anterior descending artery	74/126 (58.7%)	55/69 (79.7%)	
Non-LAD	52/126 (41.2%)	14/69 (20.3%)	
Stent diameter, mm (195/195) median (IQ)	3.0 (2.75–3.5)	3.0 (2.5–3.0)	0.012
Total stent length, mm (195/195) median (IQ)	24 (16–32)	28 (20–32)	0.062
IVUS or OCT and UFR or OFR findings			
Distal segment length ≥5 mm	116/126 (92.06%)	66/69 (95.65%)	
Distal segment length ≥10 mm	92/126 (73.02%)	55/69 (79.71%)	
Distal focal lesion			
Anatomical	5/116 (4.31%)	11/66 (16.67%)	0.005
Physiological	0/92 (0)	3/55 (5.45%)	0.024
Distal MLA, mm^2 (192/195) median (IQ)	3.88 (2.83–6.13)	3.35 (2.62–4.08)	<0.001
Distal segment length, mm (192/195) median (IQ)	11 (7.2–15.8)	11.9 (10–18.3)	0.089
Distal UFR or OFR gradient, (192/195) median (IQ)	0.01 (0–0.02)	0.02 (0.01–0.04)	<0.001
Distal UFR or OFR gradient, normalized for length (192/195)	0.01 (0–0.017)	0.018 (0.014–0.025)	<0.001
In-stent gradient (195/195)	0.02 (0.01–0.03)	0.06 (0.04–0.07)	<0.001
In-stent gradient normalized for stent length (192/195)	0.008 (0.004–0.012)	0.018 (0.014–0.024)	<0.001
MSA (mm^2)	5.7 (4.3–7.7)	4.72 (3.97–5.66)	0.001
Stent expansion index (SEI) (195/195) mean (SD)	83.87 ± 17.25	82.65 ± 17.65	0.635
Stent expansion			
SEI ≤ 80	51/126 (40.47%)	31/69 (44.93%)	
SEI ≥ 80	75/126 (59.53%)	48/69 (55.07%)	
In-stent segment length, in mm (195/195) median (IQ)[a]	27.18 ± 10.28	29.8 (20.7–38.8)	0.029
Proximal segment length ≥5 mm	101/126 (80.16%)	60/69 (86.96%)	
Proximal segment length ≥10 mm	89/126 (70.63%)	59/69 (85.51%)	
Proximal focal lesion			
Anatomical	9/101 (8.91%)	17/60 (28.33%)	
Physiological	1/89 (1.12%)	13/59 (22.03%)	
Proximal MLA, mm^2 (185/195) median (IQ)[a]	7.23 (4.8–10.1)	4.7 (3.2–6.5)	<0.001
Proximal normalized segment length, mm (185/195) median (IQ)[a]	10.6 (6.6–19.4)	18.1 (10–31.5)	<0.001
Proximal UFR or OFR gradient (185/195) median (IQ)[a]	0.01 (0–0.02)	0.05 (0.02–0.08)	<0.001
Proximal UFR or OFR gradient normalized for length (185/195)[a]	0.009 (0–0.018)	0.024 (0.016–0.034)	<0.001

IVUS, intravascular ultrasound; OCT, optical coherence tomography; OFR, optical flow ratio; UFR, ultrasonic flow ratio; SEI, stent expansion index; MLA, minimal lumen area.
[a]Results expressed in median and quartiles.

gradients, has also been previously described.[42] A focal pressure drop outside the stented segment is typically indicative of residual stenosis potentially suitable for additional PCI. Currently, intracoronary imaging is still the gold standard for high-resolution detection of sub-optimal stenting results and for guiding PCI optimization. Identification and correction of stent under-expansion, malapposition, and edge dissection as identified by OCT is one of the main contributors of improved FFR after OCT guided PCI optimization.[12]

Another potential cause of TVF that may not be detected by FFR is non-obstructive residual disease with high plaque burden. In the CLIMA (Relationship between coronary plaque morphology of the LAD artery and 12 months clinical outcome) study, the presence of physiologically non-obstructive coronary lesions with high-risk plaque features located in the proximal LAD was associated with a higher occurrence of composite endpoints including cardiac death, target-vessel MI, or target-vessel revascularization. The primary goals of assessing intracoronary physiology are evaluating the functional severity of coronary stenoses and identifying focal pressure gradients suitable for percutaneous revascularization. A comprehensive and carefully studied UFR/OFR pull back (a surrogate of physiology) before and after PCI will likely result in more personalized procedural planning, leading to better patient and vessel selection, and a higher degree of appropriately functional revascularization. Through the amalgamation of physiological and morphological assessments following PCI, we can leverage the distinctive merits inherent in each methodology, thereby enhancing overall clinical outcomes. The FLAVOUR study demonstrated that, in patients with intermediate

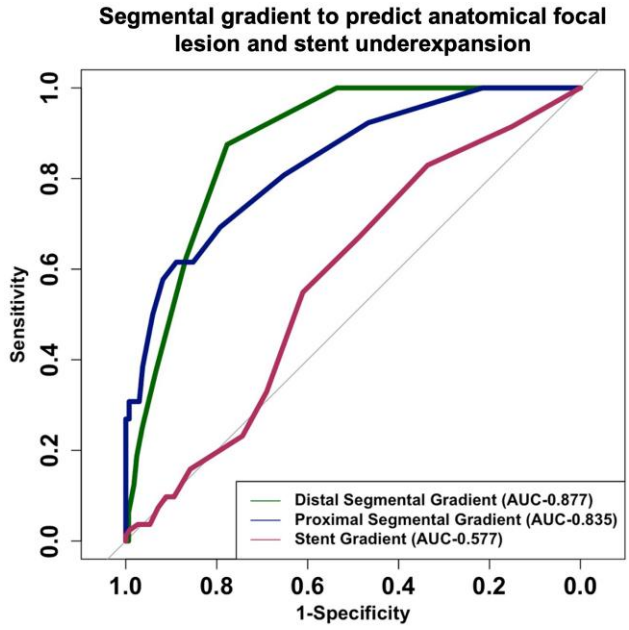


Figure 2 Discriminative ability of segmental virtual FFR gradients to predict intravascular imaging detected residual anatomical focal disease. ROC curves and AUC values for segmental virtual FFR gradients to predict distal focal, proximal focal, and stent under-expansion.

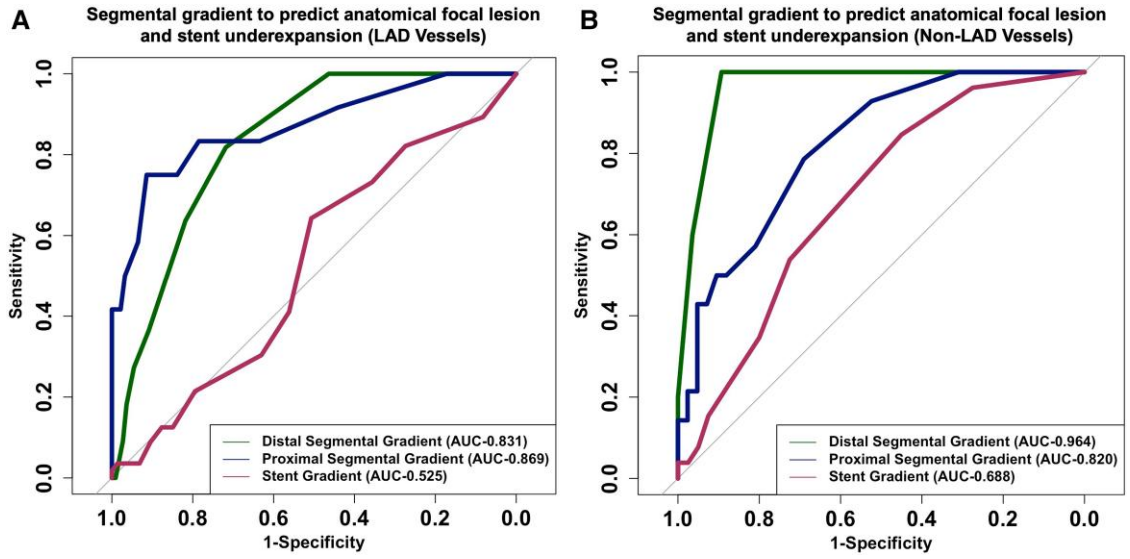


Figure 3 Discriminative ability of segmental virtual FFR gradients to predict intravascular imaging detected residual anatomical focal disease in LAD vs. non-LAD vessels. ROC curves and AUC values for segmental virtual FFR gradients to predict distal focal, proximal focal and stent under-expansion in LAD (*A*) and non-LAD vessels (*B*). FFR, fractional flow reserve; LAD, left anterior descending artery.

stenosis undergoing evaluation for PCI, FFR guidance was non-inferior to IVUS guidance concerning the composite primary outcome of death, MI, or revascularization at 24 months.[43] A FLAVOUR sub-study investigated the incidence of discrepancies between quantitative coronary angiography (QCA) and FFR or IVUS, as well as the outcomes of FFR- and IVUS-guided strategies in discordant coronary lesions.[44] The discordance rate between QCA and FFR or IVUS was 30.2% (*n* = 551). Importantly, FFR- and IVUS-guided strategies for these lesions showed comparable outcomes regarding patient-oriented composite end-points at 24 months.[44]

However, it is essential to note that the FLAVOUR study primarily compared FFR vs. IVUS for decision-making regarding revascularization and stent implantation. The potential benefits of a physiological (UFR/OFR) vs. morphological guidance approach (MLA)—including

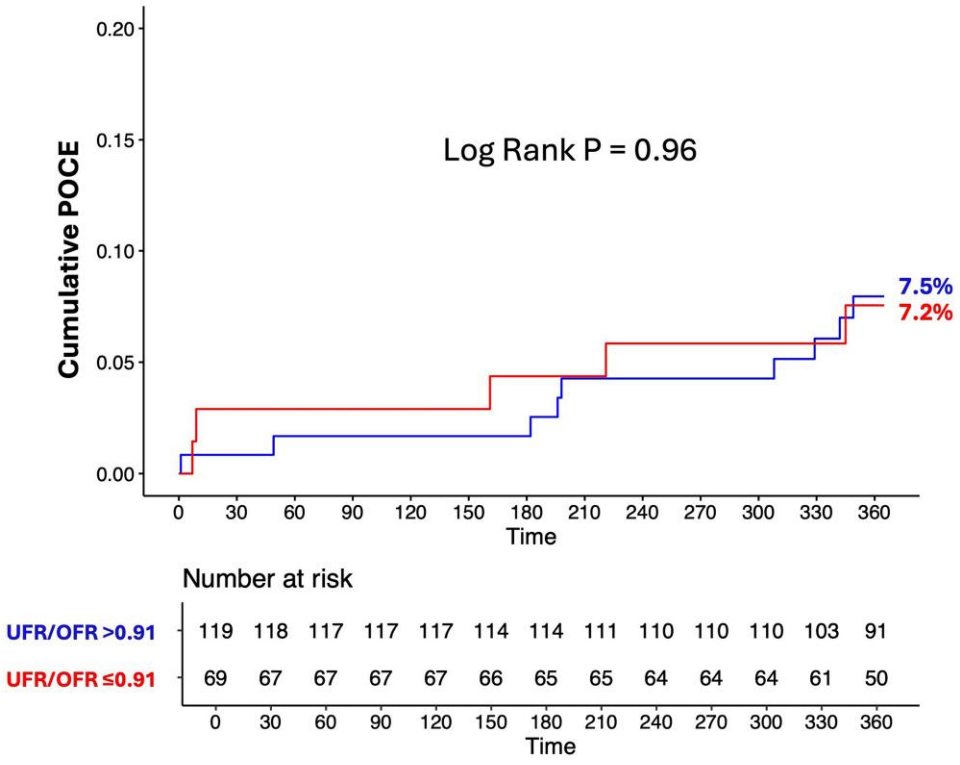


Figure 4 Relationship between a low post-PCI UFR/OFR (<0.91) and 1-year POCE. Kaplan–Meier curves show the cumulative incidence of POCE (a composite of all-cause mortality, any stroke, any MI including non-target vessel territory, and any revascularization) over 365 days of follow-up among the vessels with low (<0.91) or high (≥0.91) post-percutaneous coronary intervention (PCI) UFR/OFR value. OFR, optical flow ratio; UFR, ultrasonic flow ratio.

novel indices such as the pullback pressure gradient index—merit further exploration. Future trials could investigate these indices both before PCI to better elucidate their clinical utility. Furthermore, the potential clinical outcome benefits of a physiological guidance approach, such as UFR/OFR gradients, compared with a morphological guidance approach, such as stent expansion assessed by IVUS or OCT, warrant further investigation. Future trials should explore these strategies post-PCI to better elucidate their clinical utility.

Study limitations

First, the cross-correlation between OFR and UFR remains unknown. However, combining IVUS and OCT in the same vessel lacks justification, as both OFR and UFR have been validated against wire-based FFR and correlation between UFR and OFR in 39 vessels segments was excellent in a population with vulnerable plaque. Secondly, in some vessels distal segment lesions might have been missed due to the limited pullback length beyond the distal stent edge. Thirdly, we used only one definition for stent under-expansion and did not explore various other criteria or the correlation with stent gradient, however, prior studies indicate that stent gradient did not vary among different definitions of stent expansion.[22] Fourth, whilst there are no motorized wire-based physiology pullbacks to validate our results, we relied on virtual UFR/OFR pullback curves, validated against wire-based FFR.

Fifth, in the ASET JAPAN pilot study there was no clear guidance criteria either by physiological or morphological approach using IVUS/OCT either before or after PCI to guide revascularization. Sixth, the study included only stable patients, which raises questions about whether the findings can be generalized to non-culprit lesions in patients with acute coronary syndromes, such as NSTEMI or STEMI. The enrolled population was very low anatomical risk (mean anatomic SYNTAX score—8). The majority of patients had total stent lengths ranging from 20 to 30 mm, and the study included minimal cases involving PCI of the left main coronary artery, chronic total occlusions, or bifurcation lesions. This restricts the applicability of the findings to patients with more complex coronary anatomy. Additionally, the patient cohort was low-risk from a clinical standpoint, as most patients had preserved left ventricular ejection fraction (Mean LVEF—60.5%) and relatively low prevalence of peripheral artery disease, prior PCI, or coronary artery bypass grafting. Whether the results extend to higher-risk patients both anatomically and clinically remains to be determined. Finally, we also did not observe any significant difference in clinical outcomes between patients with and without sub-optimal physiological outcomes as assessed by OFR/UFR. However, given the very low anatomical and clinical risk of the study population, it is likely that clinical events will accrue over time. Therefore, longer-term follow-up is necessary to discern potential differences in clinical outcomes, as the current analysis only includes clinical follow-up up to 1 year

Supplementary data

Supplementary data are available at *European Heart Journal - Imaging Methods and Practice* online.

Consent

The certified review board (CRB), central ethics committee and local ethics committee at each participating centre approved the study protocol (Reference no. CRB4180003). All enrolled patients provided written informed consent, and the study complied with the declaration of Helsinki.

Conflict of interest: Dr Miyashita reports research grants from OrbusNeich Medical K. K., outside the submitted work. Dr Kotoku has received a grant for studying overseas from Fukuda Foundation for Medical Technology. Dr Muramatsu has received honoraria from Boston Scientific Japan and Daiichi Sankyo. Dr Tanabe reports honorarium for lectures from Boston Scientific and Daiichi Sankyo. Dr Kozuma reports honorarium for lectures from Boston Scientific, Abbott Medical, Medtronic, and scholarship funds from Boston Scientific and Abbott Medical. Dr Tu is a co-founder of Pulse Medical and received institutional research grants from Pulse Medical. Dr Serruys reports consultancy for Sahajanand Medical Technologies (SMT), Meril Life Sciences, Philips, Xeltis, outside the submitted work. Dr Onuma reports consultancy for SMT, Meril Life Sciences, Philips, Xeltis, outside the submitted work. All other authors have reported that they have no relationship relevant to the contents of this paper to disclose.

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Data availability

All data are incorporated into the article and its online supplementary material

Lead author biography

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References

1. De Bruyne B, Pijls NH, Kalesan B, Barbato E, Tonino PA, Piroth Z *et al.* Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med* 2012;**367**:991–1001.
2. Pijls NH, Fearon WF, Tonino PA, Siebert U, Ikeno F, Bornschein B *et al.* Fractional flow reserve versus angiography for guiding percutaneous coronary intervention in patients with multivessel coronary artery disease: 2-year follow-up of the FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study. *J Am Coll Cardiol* 2010;**56**:177–84.
3. Jeremias A, Davies JE, Maehara A, Matsumura M, Schneider J, Tang K *et al.* Blinded physiological assessment of residual ischemia after successful angiographic percutaneous coronary intervention: the DEFINE PCI study. *JACC Cardiovasc Interv* 2019;**12**:1991–2001.
4. Diletti R, Masdjedi K, Daemen J, van Zandvoort LJ, Neleman T, Wilschut J *et al.* Impact of poststenting fractional flow reserve on long-term clinical outcomes: the FFR-SEARCH study. *Circ Cardiovasc Interv* 2021;**14**:e009681.
5. Piroth Z, Toth GG, Tonino PA, Barbato E, Aghlmandi S, Curzen N *et al.* Prognostic value of fractional flow reserve measured immediately after drug-eluting stent implantation. *Circ Cardiovasc Interv* 2017;**10**:e005233.
6. Patel MR, Jeremias A, Maehara A, Matsumura M, Zhang Z, Schneider J *et al.* 1-Year outcomes of blinded physiological assessment of residual ischemia after successful PCI: DEFINE PCI trial. *JACC Cardiovasc Interv* 2022;**15**:52–61.
7. Zhang J, Gao X, Kan J, Ge Z, Han L, Lu S *et al.* Intravascular ultrasound versus angiography-guided drug-eluting stent implantation: the ULTIMATE trial. *J Am Coll Cardiol* 2018;**72**:3126–37.
8. van Zandvoort LJC, Masdjedi K, Witberg K, Ligthart J, Tovar Forero MN, Diletti R *et al.* Explanation of postprocedural fractional flow reserve below 0.85. *Circ Cardiovasc Interv* 2019;**12**:e007030.
9. Kedhi E, Berta B, Roleder T, Hermanides RS, Fabris E, IJsselmuiden AJ *et al.* Thin-cap fibroatheroma predicts clinical events in diabetic patients with normal fractional flow reserve: the COMBINE OCT-FFR trial. *Eur Heart J* 2021;**42**:4671–9.
10. Räber L, Mintz GS, Koskinas KC, Johnson TW, Holm NR, Onuma Y *et al.* Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions. *Eur Heart J* 2018;**39**:3281–300.
11. Yu W, Tanigaki T, Ding D, Wu P, Du H, Ling L *et al.* Accuracy of intravascular ultrasound-based fractional flow reserve in identifying hemodynamic significance of coronary stenosis. *Circ Cardiovasc Interv* 2021;**14**:e009840.
12. Ding D, Yu W, Tauzin H, De Maria GL, Wu P, Yang F *et al.* Optical flow ratio for assessing stenting result and physiological significance of residual disease. *EuroIntervention* 2021;**17**:e989–98.
13. Yu W, Huang J, Jia D, Chen S, Raffel OC, Ding D *et al.* Diagnostic accuracy of intracoronary optical coherence tomography-derived fractional flow reserve for assessment of coronary stenosis severity. *EuroIntervention* 2019;**15**:189–97.
14. Huang J, Emori H, Ding D, Kubo T, Yu W, Huang P *et al.* Diagnostic performance of intracoronary optical coherence tomography-based versus angiography-based fractional flow reserve for the evaluation of coronary lesions. *EuroIntervention* 2020;**16**:568–76.
15. Emori H, Kubo T, Shiono Y, Ino Y, Shimamura K, Terada K *et al.* Comparison of optical flow ratio and fractional flow ratio in stent-treated arteries immediately after percutaneous coronary intervention. *Circ J* 2020;**84**:2253–8.
16. Yang C, Sui YG, Shen JY, Guan CD, Yu W, Tu SX *et al.* Diagnostic performance of ultrasonic flow ratio versus quantitative flow ratio for assessment of coronary stenosis. *Int J Cardiol* 2024;**400**:131765.
17. Jeremias A, Maehara A, Matsumura M, Shlofmitz RA, Maksoud A, Akasaka T *et al.* Optical coherence tomography-based functional stenosis assessment: FUSION-A prospective multicenter trial. *Circ Cardiovasc Interv* 2024;**17**:e013702.
18. Masuda S, Muramatsu T, Ishibashi Y, Kozuma K, Tanabe K, Nakatani S *et al.* Reduced-dose prasugrel monotherapy without aspirin after PCI with the SYNERGY stent in East Asian patients presenting with chronic coronary syndromes or non-ST-elevation acute coronary syndromes: rationale and design of the ASET Japan pilot study. *AsiaIntervention* 2023;**9**:39–48.
19. Muramatsu T, Masuda S, Kotoku N, Kozuma K, Kawashima H, Ishibashi Y *et al.* Prasugrel monotherapy after percutaneous coronary intervention with biodegradable-polymer platinum-chromium everolimus eluting stent for Japanese patients with chronic coronary syndrome (ASET-JAPAN). *Circ J* 2023;**87**:857–65.
20. Scarsini R, Fezzi S, Leone AM, De Maria GL, Pighi M, Marcoli M *et al.* Functional patterns of coronary disease: diffuse, focal, and serial lesions. *JACC Cardiovasc Interv* 2022;**15**:2174–91.
21. Biscaglia S, Uretsky BF, Tebaldi M, Erriquez A, Brugaletta S, Cerrato E *et al.* Angio-Based fractional flow reserve, functional pattern of coronary artery disease, and prediction of percutaneous coronary intervention result: a proof-of-concept study. *Cardiovasc Drugs Ther* 2022;**36**:645–53.
22. Neleman T, Scoccia A, Groenland FTW, Ziedses des Plantes AC, van Zandvoort LJC, Ligthart JMR *et al.* Validation of segmental post-PCI physiological gradients with IVUS-detected focal lesions and stent underexpansion. *JACC Cardiovasc Interv* 2023;**16**:1763–73.
23. Ben-Dor I, Torguson R, Gaglia MA, Gonzalez J, Maluenda MA, Bui G *et al.* Correlation between fractional flow reserve and intravascular ultrasound lumen area in intermediate coronary artery stenosis. *EuroIntervention* 2011;**7**:225–33.
24. Lee CH, Tai BC, Soon CY, Low AF, Poh KK, Yeo TC *et al.* New set of intravascular ultrasound-derived anatomic criteria for defining functionally significant stenoses in small coronary arteries (results from Intravascular Ultrasound Diagnostic Evaluation of Atherosclerosis in Singapore [IDEAS] study). *Am J Cardiol* 2010;**105**:1378–84.
25. Fujimura T, Matsumura M, Witzenbichler B, Metzger DC, Rinaldi MJ, Duffy PL *et al.* Stent expansion indexes to predict clinical outcomes: an IVUS substudy from ADAPT-DES. *JACC Cardiovasc Interv* 2021;**14**:1639–50.
26. van Nunen LX, Zimmermann FM, Tonino PA, Barbato E, Baumbach A, Engstrøm T *et al.* Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial. *Lancet* 2015;**386**:1853–60.

27. Tonino PA, De Bruyne B, Pijls NH, Siebert U, Ikeno F, van' t Veer M *et al.* Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med* 2009;**360**:213–24.
28. Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM, Bischoff JM *et al.* 2021 ACC/AHA/SCAI Guideline for coronary artery revascularization: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2022;**145**:e4–17.
29. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U *et al.* 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J* 2019;**40**:87–165.
30. Hong SJ, Mintz GS, Ahn CM, Kim JS, Kim BK, Ko YG *et al.* Effect of intravascular ultrasound-guided drug-eluting stent implantation: 5-year follow-up of the IVUS-XPL randomized trial. *JACC Cardiovasc Interv* 2020;**13**:62–71.
31. Lee JM, Choi KH, Song YB, Lee JY, Lee SJ, Lee SY *et al.* Intravascular imaging-guided or angiography-guided complex PCI. *N Engl J Med* 2023;**388**:1668–79.
32. Serruys PW, Kogame N, Onuma Y. Was the ball inside or outside the court?: ask the hawk-eye system. *JACC Cardiovasc Interv* 2019;**12**:2089–92.
33. Collison D, Didagelos M, Aetesam-ur-Rahman M, Copt S, McDade R, McCartney P *et al.* Post-stenting fractional flow reserve vs coronary angiography for optimization of percutaneous coronary intervention (TARGET-FFR). *Eur Heart J* 2021;**42**:4656–68.
34. van Zandvoort LJ, Ali Z, Kern M, van Mieghem NM, Mintz GS, Daemen J. Improving PCI outcomes using postprocedural physiology and intravascular imaging. *Cardiovascular Interventions* 2021;**14**:2415–30.
35. Johnson NP, Collet C. Can FFR after stenting help reduce target vessel failure? *JACC Cardiovasc Interv* 2021;**14**:1901–3.
36. Li SJ, Ge Z, Kan J, Zhang JJ, Ye F, Kwan TW *et al.* Cutoff value and long-term prediction of clinical events by FFR measured immediately after implantation of a drug-eluting stent in patients with coronary artery disease: 1- to 3-year results from the DKCRUSH VII registry study. *JACC Cardiovasc Interv* 2017;**10**:986–95.
37. Ahn SG, Hong S, Son JW, Lee JW, Youn YJ, Ahn MS *et al.* Validation of post-stenting fractional flow reserve with intravascular ultrasound parameters for optimal stent deployment. *Int J Cardiovasc Imaging* 2020;**36**:197–203.
38. Doh JH, Nam CW, Koo BK, Lee SY, Choi H, Namgung J *et al.* Clinical relevance of poststent fractional flow reserve after drug-eluting stent implantation. *J Invasive Cardiol* 2015;**27**:346–51.
39. Fearon WF, Luna J, Samady H, Powers ER, Feldman T, Dib N *et al.* Fractional flow reserve compared with intravascular ultrasound guidance for optimizing stent deployment. *Circulation* 2001;**104**:1917–22.
40. Reith S, Battermann S, Hellmich M, Marx N, Burgmaier M. Correlation between OCT-derived intrastent dimensions and fractional flow reserve measurements after coronary stent implantation and impact on clinical outcome. *J Invasive Cardiol* 2015;**27**:222–8.
41. Baranauskas A, Peace A, Kibarskis A, Shannon J, Abraitis V, Bajoras V *et al.* FFR result post PCI is suboptimal in long diffuse coronary artery disease. *EuroIntervention* 2016;**12**:1473–80.
42. Uretsky BF, Agarwal SK, Vallurupalli S, Al-Hawwas M, Hasan R, Miller K *et al.* Prospective evaluation of the strategy of functionally optimized coronary intervention. *J Am Heart Assoc* 2020;**9**:e015073.
43. Koo BK, Hu X, Kang J, Zhang J, Jiang J, Hahn JY *et al.* Fractional flow reserve or intravascular ultrasonography to guide PCI. *N Engl J Med* 2022;**387**:779–89.
44. Lee JH, Ahn SG, Jeon HS, Lee JW, Youn YJ, Zhang J *et al.* Discordance between angiographic assessment and fractional flow reserve or intravascular ultrasound in intermediate coronary lesions: a post-hoc analysis of the FLAVOUR trial. *Korean Circ J* 2024;**54**:485–96.