Prognostic Value of Fractional Flow Reserve Measured Immediately After Drug-Eluting Stent Implantation

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Background—The predictive value of fractional flow reserve (FFR) measured immediately after percutaneous coronary intervention (PCI) with drug-eluting stent placement has not been prospectively investigated. We investigated the potential of post-PCI FFR measurements to predict clinical outcome in patients from FAME 1 and 2 trials (Fractional Flow Reserve or Angiography for Multivessel Evaluation).

Methods and Results—All patients of FAME 1 and FAME 2 who had post-PCI FFR measurement were included. The primary outcome was vessel-oriented composite end point at 2 years, defined as vessel-related cardiovascular death, vessel-related spontaneous myocardial infarction, and ischemia-driven target vessel revascularization. Eight hundred thirty-eight vessels in 639 patients were analyzed. Baseline FFR values did not differ between vessels with versus without vessel-oriented composite end point (0.66±0.11 versus 0.63±0.14, respectively; *P*=0.207). Post-PCI FFR was significantly lower in vessels with vessel-oriented composite end point (0.88±0.06 versus 0.90±0.06, respectively; *P*=0.019). Comparing the 2-year outcome of lower and upper tertiles of post-PCI FFR significant difference was found favoring upper tertile in terms of overall vessel-oriented composite end point (9.2% versus 3.8%, respectively; hazard ratio, 1.46; 95% confidence interval, 1.02–2.08; *P*=0.037) and target vessel revascularization (7.0% versus 2.4%, respectively; hazard ratio, 1.59; 95% confidence interval, 1.03–2.46; *P*=0.037). When adjusted to sex, hypertension, diabetes mellitus, target vessel, serial stenosis, and baseline percentage diameter stenosis, a strong trend was preserved in terms of target vessel revascularization (harzard ratio, 1.55; 95% confidence interval, 0.97–2.46; *P*=0.066), favoring the upper tertile. Post-PCI FFR of 0.92 was found to have the highest diagnostic accuracy; however, the positive likelihood ratio remained low (<1.4).

Conclusions—A higher post-PCI FFR value is associated with a better vessel-related outcome. However, its predictive value is too low to advocate its use as a surrogate clinical end point. **(*Circ Cardiovasc Interv*. 2017;10:e005233. DOI: 10.1161/CIRCINTERVENTIONS.116.005233.)**

Key Words: acute coronary syndrome ■ drug-eluting stent ■ hospitalization ■ myocardial infarction ■ percutaneous coronary intervention

On the basis of robust scientific[1,2] and clinical outcome data derived from large randomized controlled trials and registries,[3–18] fractional flow reserve (FFR) has become the standard for clinical decision making about percutaneous coronary revascularization.[19] FFR has a Class I indication with a level of evidence A in stable patients to identify hemodynamically significant coronary lesions when evidence of ischemia is not available.[19] Recent prospective outcome data, obtained in medically treated patients, indicated a risk continuum for FFR values from 0 to 1, where the lower the FFR the higher the long-term event rate.[18,20] However, it is still unclear whether a similar correlation is maintained after revascularization because the clinical value of FFR to evaluate the results of percutaneous coronary intervention (PCI) has not been prospectively investigated in the drug-eluting stent (DES) era.

Accordingly, we investigated the potential of post-PCI FFR measurements to predict clinical outcome in a large cohort of patients enrolled in the FAME trials.

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WHAT IS KNOWN

- Fractional flow reserve with a clear cutoff value of 0.80 is the current gold standard for invasive hemodynamic evaluation of coronary stenoses.
- True prognostic value of fractional flow reserve, measured right after percutaneous coronary intervention with drug-eluting stent is unknown.

WHAT THE STUDY ADDS

- Low post–percutaneous coronary intervention fractional flow reserve is associated with worse long-term clinical outcome on vessel level.
- However, after percutaneous coronary intervention, there is no well-defined fractional flow reserve cutoff value, which could be applied for individual clinical decisions or used as surrogate end point in future studies.

Methods

Patients

The design and results of the FAME 1 and FAME 2 studies have been reported previously.[5–7,9] Both are international, multicenter, prospective, randomized clinical trials with comparable inclusion and exclusion criteria. In brief, the FAME 1 trial enrolled patients with angiographic multivessel coronary artery disease amenable for PCI. Patients were randomized either to an FFR-guided or to an angiography-guided approach. In the FFR-guided arm, only lesions with an FFR ≤0.80 were treated by PCI, whereas in the angiography-guided arm, all narrowings with ≥50% diameter stenosis (DS) were treated by PCI. Stenting was performed using first-generation DES. The primary end point was the composite of all-cause death, nonfatal myocardial infarction (MI), and any repeat revascularization (major adverse cardiac events [MACE]) at 1 year as adjudicated by a clinical event committee. A prespecified secondary end point of the study was the MACE rate at 2 years.[17] The FAME 2 trial enrolled patients with stable angina, stabilized acute coronary syndrome or silent ischemia with 1, 2, or 3-vessel disease. Patients having at least one stenosis with an FFR ≤0.80 were randomized to FFR-guided PCI plus best available medical therapy or best available medical therapy alone. PCI was performed using second-generation DES. The primary end point of the study was a composite of all-cause death, nonfatal MI, and unplanned hospitalization leading to urgent revascularization at 2 years. A prespecified secondary end point of the study was any repeat revascularization at 2 years.[7] In both trials, patients were included only if there was at least one clearly identifiable focal narrowing at angiography deemed to be amenable for stenting. Patients with only diffuse disease were not considered for the study as it was supposed that no local treatment (stenting) might significantly improve vessel hemodynamics.

The present analysis includes all patients who had post-PCI FFR measurement from the FFR-guided arm of the FAME 1 trial and the PCI plus best available medical therapy arm of the FAME 2 trial. Obtaining post-PCI FFR was not mandated per protocol. Institutional research board has approved the present study. All patients gave informed consent before enrollment to FAME 1 or FAME 2 trials.

Vessels

The present study investigated the relationship between post-PCI FFR values and clinical outcome at vessel level. All angiographic characteristics and end points are reported at vessel level. Coronary stenosis severity was assessed by visual estimation and reported, according to the main trials, in the following strata of DS: <50%, 50% to 69%, 70% to 90%, and >90%.

Table 1. Clinical Characteristics of the Patient Population

	Total	FAME 1	FAME 2	*P* Value
Patients out of the study, n (%)	639 (67)	352 (69)	287 (64)	0.232
Age, y (mean±SD)	64±10	65±10	63±9	0.114
BMI, kg/m^2 (mean±SD)	28±5	28±5	28±4	0.618
Male sex, n (%)	506 (79)	281 (80)	225 (78)	0.906
Hypertension, n (%)	435 (68)	211 (68)	224 (78)	**<0.001**
Dyslipidemia, n (%)	472 (74)	254 (72)	218 (76)	0.554
Diabetes mellitus, n (%)	159 (25)	81 (23)	78 (27)	0.480
Smoker, n (%)	152 (24)	94 (27)	58 (20)	0.159
Family history, n (%)	271 (42)	135 (38)	136 (47)	0.071
Previous PCI, n (%)	145 (23)	90 (26)	55 (19)	0.158
Previous MI, n (%)	284 (37)	127 (36)	111 (39)	0.796
CCS				
1	171 (27)	91 (26)	80 (28)	
2	251 (39)	116 (33)	135 (47)	
3	143 (22)	94 (27)	49 (17)	
4	74 (12)	51 (14)	23 (8)	**0.002**

Comparison of population from FAME 1 and FAME 2 trials. BMI indicates body mass index; CCS, Canadian Cardiovascular Society; FAME, Fractional Flow Reserve or Angiography for Multivessel Evaluation; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

End Points

Follow-up was censored 2 years after enrollment or at the time of death. The primary end point of the present analysis is the vessel-oriented composite end point (VOCE) at 2 years, defined as the composite of vessel-related cardiovascular death, vessel-related spontaneous (ie, nonperiprocedural) MI, and ischemia-driven target vessel revascularization (TVR, both urgent and nonurgent). All events were adjudicated by an independent clinical event committee, blinded to randomization allocation. For the present analysis, all the original narratives were reviewed and evaluated independently by 2 interventional cardiologists (Z.P. and G.G.T.), blinded to baseline clinical and procedural characteristics, as well as to post-PCI FFR value. Events were designated as vessel-related or not vessel-related.

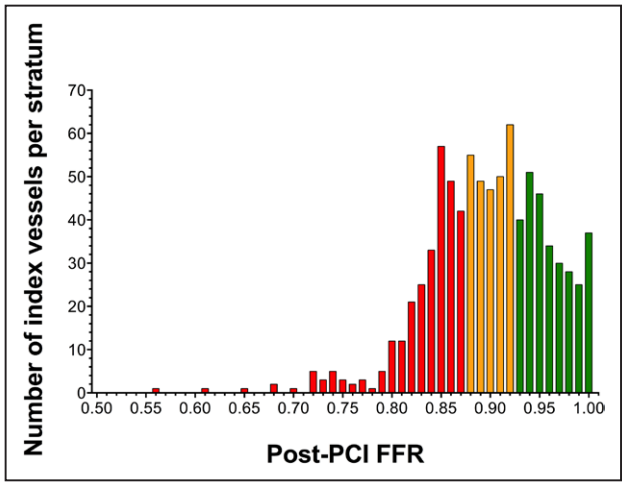

Figure 1. Distribution of post–percutaneous coronary intervention (PCI) fractional flow reserve (FFR) values. Colors indicate the lower (<0.88; red), the middle (0.88–0.92; orange), and the upper (>0.92; green) tertiles according to post-PCI FFR groups.

Table 2. Angiographic, Functional, and Procedural Characteristics of the Index Vessels

	Total (n=838)	FAME 1 (n=505)	FAME 2 (n=333)	*P* Value
Target vessel, n (%)				
LAD	433 (52)	229 (45)	204 (61)	
LCx	188 (22)	124 (25)	64 (19)	
RCA	217 (26)	152 (30)	65 (20)	**<0.001**
Baseline diameter stenosis, n (%)				
<50%	23 (3)	21 (4)	2 (1)	
50%–70%	287 (34)	174 (34)	113 (34)	
71%–90%	397 (47)	216 (43)	181 (54)	
>90%	127 (15)	90 (18)	37 (12)	**<0.001**
Serial stenoses, n (%)	225 (26)	195 (38)	30 (9)	**<0.001**
Baseline FFR, mean±SD	0.63±0.14	0.61±0.15	0.67±0.12	**<0.001**
No. of stents, mm, mean±SD	1.3±0.6	1.3±0.6	1.3±0.6	0.696
Total stent length, mm, mean±SD	23±13	23±12	27±14	**<0.001**
Post-PCI FFR; mean±SD	0.90±0.06	0.90±0.07	0.90±0.06	0.595

Comparison of population from the FAME 1 and FAME 2 trials. FAME indicates Fractional Flow Reserve or Angiography for Multivessel Evaluation; FFR, fractional flow reserve; LAD, left anterior descending; LCx, left circumflex; PCI, percutaneous coronary intervention; and RCA, right coronary artery.

In case of disagreement, the narrative was reviewed again until a joint agreement was met. Death was categorized as either cardiovascular or noncardiovascular. Any death of unknown cause was counted as cardiovascular. Cardiovascular death in patients with multiple index stenoses was assigned to each index stenosis. Any spontaneous MI without clearly identifiable culprit vessel was counted as target vessel related. Any spontaneous MI in patients with multiple index stenoses without clearly identifiable culprit vessel was assigned to each index stenosis.

Statistical Analysis

Continuous variables are presented as mean±SD or median and interquartile range from the 25th to the 75th percentile; categorical data are presented as numbers and percentages, as appropriate. Normal distribution was tested with D'Agostino K2 test. Comparisons between continuous variables were performed using Student *t* test or Mann–Whitney test, as appropriate. Comparisons between categorical variables were evaluated using Pearson χ^2 or Fisher exact test, as appropriate. The predictive value of clinical and angiographic parameters on post-PCI FFR was determined by deriving the β-coefficient in a generalized linear mixed-effects regression model after standardization to achieve that the variance of dependent and independent variable was 1. Sensitivity, specificity, and optimal diagnostic cutoff values were defined from the calculated receiver–operator characteristic curves, as appropriate. In lesion-level–based analysis, general procedural characteristics and generalized mixed-effects models were used with patient identification as random effect to account for the nonindependence of lesions within the same patient. The multilevel mixed-effects model used for lesion-level analyses fitted random intercepts to account for the correlation of characteristics of lesions within patients. In analysis of time-to-event outcomes, Cox regression was used with robust SE to account for the correlation between lesions. Proportional-hazards test based on Schoenfeld residuals was performed after fitting a crude and adjusted survival model. (Table I in the Data Supplement) The added predictive ability of the new predictor (baseline FFR) over and above a reference model (post-PCI FFR) was assessed by integrated discrimination improvement index based on logistic model.[21] Kaplan–Meier curves were constructed for the primary end point of VOCE at 2-year follow-up. Two sided *P* values were reported throughout and *P* values smaller than 0.05 were considered as statistically significant. Analyses were performed with Prism GraphPad 5.0 (GraphPad Software, Inc, CA), SPSS 20.0 (IBM, Inc, New York), and Stata 14.0 (Stata Corp, College Station, TX).

Results

Patients and Vessels

Of the 509 patients randomized to the FFR-guided arm in the FAME 1 trial, 352 had post-PCI FFR measurement (69.2%). Of the 447 patients randomized to PCI plus medical therapy in the FAME 2 trial, 287 (64.2%) had post-PCI FFR measurement. Together, these 639 patients constitute the study group of the present analysis. The baseline characteristics of the patient group are summarized in Table 1. Patients from the FAME 1 and FAME 2 trials were similar, except for the higher rate of hypertension and more imbalanced angina severity as defined by the Canadian Cardiovascular Society classification in the FAME 2 population.

In these 639 patients, 838 vessels were evaluated in the present analysis, of which 433 (51.7%) were left anterior descending (LAD), 217 (25.9%) were right coronary arteries, and 188 (22.4%) were circumflex arteries. The median value of baseline FFR measurements was 0.68 (0.54–0.74): 0.69 (0.58–0.75) in the LAD, 0.66 (0.50–0.74) in the circumflex

Table 3. Predictive Value of Different Clinical and Angiographic Characteristics on the Post-PCI FFR Value

Variable	Unstandardized, β	95% CI	Standardized Coefficient, β	95% CI	*P* Value
Male sex	–0.017	–0.028 to –0.007	–0.113	–0.182 to –0.044	**0.001**
Diabetes mellitus	–0.011	–0.021 to –0.001	–0.079	–0.148 to –0.009	**0.026**
LAD stenosis	–0.043	–0.051 to –0.035	–0.340	–0.403 to –0.277	**<0.001**
Baseline DS	0.013	0.007 to 0.018	0.156	0.090 to 0.223	**<0.001**
Baseline FFR	0.036	0.006 to 0.066	0.081	0.014 to 0.148	**0.019**
No. of stents	–0.007	–0.014 to 0.001	–0.067	–0.134 to 0.001	0.052

CI indicates confidence interval; DS, diameter stenosis; FFR, fractional flow reserve; LAD, left anterior descending; and PCI, percutaneous coronary intervention.

arteries, and 0.64 (0.50–0.74) in the right coronary arteries. The median value of post-PCI FFR measurements was 0.90 (0.86–0.94). The distribution is indicated in Figure 1. Detailed lesion and procedural characteristics are reported in Table 2. No relationship was found between baseline FFR and post-PCI FFR values (Figure I in the Data Supplement). Lesions were more frequently located in the LAD. However, serial stenoses occurred more often in the FAME 1 trial in which mean baseline FFR was also lower. Still, the mean post-PCI FFR value was similar between the 2 study populations.

By computing standardized coefficient in multiple regression analysis, male sex, diabetes mellitus, and LAD location were found as significant predictors of a lower post-PCI FFR value, whereas use of multiple stents in the given vessel showed a strong trend to predict lower post-PCI FFR value. Higher baseline DS and higher baseline FFR predict higher post-PCI FFR value (Table 3). Comparison between extended (post-PCI FFR+baseline FFR) and reference (post-PCI FFR alone) models shows that there is a small difference between their predictive ability (integrated discrimination improvement=0.00565; z=2.53; P=0.012).

Clinical Follow-Up

Complete follow-up was obtained for 93.8% of the patients. The mean follow-up was 23.6±2.8 months (time to censored event between 0 and 24 months). Altogether, 69 events were detected in 58 treated vessels (6.9%). The distribution is indicated in Figure 2. Baseline FFR values did not differ between vessels with versus without VOCE (0.66; 95% confidence interval [CI], 0.63–0.69 versus 0.63; 95% CI, 0.62–0.64, respectively; P=0.207). Post-PCI FFR was significantly lower in vessels with VOCE during follow-up (0.88; 95% CI, 0.87–0.90 versus 0.90; 95% CI, 0.89–0.90, respectively; P=0.019).

When grouping the vessels in tertiles according to the post-PCI FFR value (<0.88 versus 0.88–0.92 versus >0.92; Table 4), a significant difference was found in the rate of VOCE with lowest incidence in the upper tertile (9.2% versus 7.9% versus 3.8%, respectively; P=0.029).

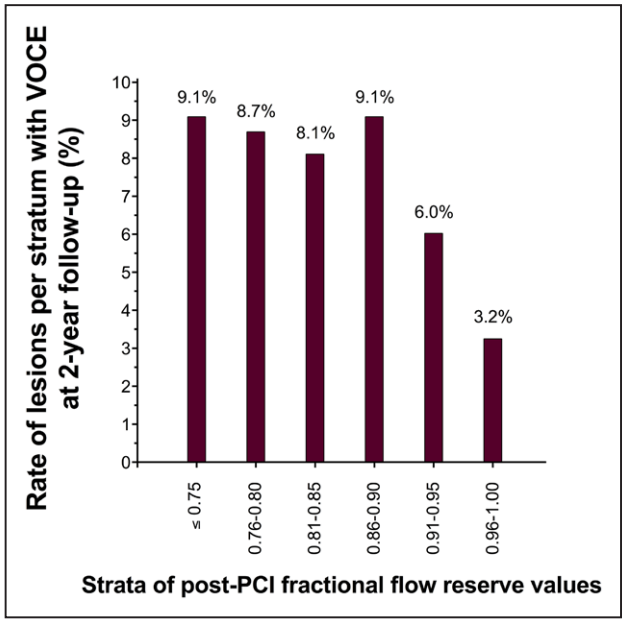

Figure 2. Rate of lesions with vessel-oriented composite end point (VOCE) in the different post–percutaneous coronary intervention (PCI) fractional flow reserve strata.

Table 4. Clinical, Angiographic, Functional, and Procedural Characteristics

	Lower (n=284)	Middle (n=263)	Upper (n=291)	*P* Value
Male sex, n (%)	241 (85)	203 (77)	224 (77)	**0.031**
Age, y, mean±SD	64±10	64±10	64±10	0.876
BMI, kg/m^2, mean±SD	28±4	28±5	28±4	0.898
HTN, n (%)	209 (74)	167 (64)	189 (65)	0.128
HLP, n (%)	216 (76)	193 (74)	223 (77)	0.902
DM, n (%)	82 (29)	65 (25)	55 (19)	0.059
Smoker, n (%)	59 (21)	65 (25)	72 (24)	0.520
Family history, n (%)	127 (45)	92 (35)	135 (47)	**0.015**
CCS, n (%)				
0	12 (4)	12 (5)	12 (4)	
1	58 (20)	56 (21)	70 (24)	
2	107 (38)	108 (41)	113 (39)	
3	71 (25)	60 (23)	58 (20)	
4	36 (13)	27 (10)	38 (13)	0.811
Vessel, n (%)				
LAD	200 (70)	156 (59)	77 (26)	
RCA	58 (20)	62 (24)	97 (33)	
LCx	26 (9)	45 (17)	117 (40)	**<0.001**
First-generation DES, n (%)	170 (60)	143 (54)	192 (66)	**0.020**
Baseline FFR, mean±SD	0.62±0.13	0.65±0.13	0.62±0.15	**0.016**
Serial stenoses, n (%)	93 (33)	61 (23)	71 (24)	**0.031**
Baseline DS, n (%)				
<50%	12 (4)	8 (3)	6 (2)	
50%–70%	112 (39)	107 (40)	68 (23)	
70%–90%	128 (45)	112 (43)	157 (54)	
>90%	32 (11)	36 (14)	29 (20)	**<0.001**
No. of stents, mean±SD	1.4±0.6	1.3±0.6	1.3±0.6	0.208
Total stent length, mean±SD	24±14	26±14	25±11	0.580
Post-PCI FFR, mean±SD	0.83±0.05	0.90±0.02	0.96±0.02	

Various characteristics of the index vessels in the lower (<0.88), the middle (0.88–0.92), and the upper (>0.92) tertiles according to post-PCI FFR. BMI indicates body mass index; CCS, Canadian Cardiovascular Society; DES, drug-eluting stent; DM, diabetes mellitus; DS, diameter stenosis; FFR, fractional flow reserve; HLP, hyperlipidemia; HTN, hypertension; LAD, left anterior descending; LCx, left circumflex; PCI, percutaneous coronary intervention; and RCA, right coronary artery.

Comparing the 2-year outcome of lower and upper tertiles of post-PCI FFR, a significant difference was found favoring the upper tertile in terms of overall VOCE (9.2% versus 3.8%, respectively; hazard ratio [HR], 1.46; 95% CI, 1.02–2.08; P=0.037) and TVR (7.0% versus 2.4%, respectively; HR,

1.59; 95% CI, 1.03–2.46; *P*=0.037). No difference was found in vessel-related spontaneous MI or in vessel-related mortality. Comparing the 2-year outcome of middle and upper tertiles of post-PCI FFR, no significant difference was found in overall VOCE, TVR, spontaneous MI, or vessel-related mortality (Figure 3; Table 5).

When adjusted to sex, hypertension, diabetes mellitus, target vessel, serial stenosis, and baseline percentage DS, a strong trend was preserved in terms of TVR (HR, 1.55; 95% CI, 0.97–2.46; *P*=0.066) favoring the upper tertile compared with the lower, as shown in Table 5.

Definition of a Potential Cutoff Value

Receiver–operator characteristic curve analysis was performed to identify a potential cutoff with prognostic value for VOCE during 2-year follow-up (Figure 4). Post-PCI FFR <0.92 has the highest Youden index. Accordingly, when comparing the 2-year outcome of vessels with post-PCI FFR <0.92 and vessels with post-PCI FFR ≥0.92, a significant difference was found in terms of overall VOCE (8.7% versus 4.2%, respectively; HR, 2.14; 95% CI, 1.19–3.84; *P*=0.011). The difference remained significant even after adjusting to sex, diabetes mellitus, target vessel, baseline percentage DS, and use of first-generation DES (HR, 1.87; 95% CI, 1.01–3.46; *P*=0.045). Yet, sensitivity and specificity of this 0.92 post-PCI FFR cutoff value to predict vessel-related events are low: 75.4% (95% CI, 62.2–85.9) and 43.3% (95% CI, 39.8–46.8), respectively. Accordingly, no post-PCI FFR value was found to have a HR >1.5 for VOCE at 2 years.

Discussion

Summary of Findings

The present study analyzes the relationship between the post-PCI FFR value immediately after DES implantation and the vessel-related events. The main findings of the present analysis can be summarized as follows:

1. Vessels with a lower residual FFR after PCI with implantation of at least one DES had significantly more clinical events compared with vessels with higher post-PCI FFR values. The difference was preserved as a strong trend even after adjustment for various clinical, angiographic, and procedural characteristics. Therefore, these findings extend the overall prognostic value of FFR to post-PCI measurements.
2. Male sex, diabetes mellitus, LAD lesion location, and the use of multiple stents are associated with a lower

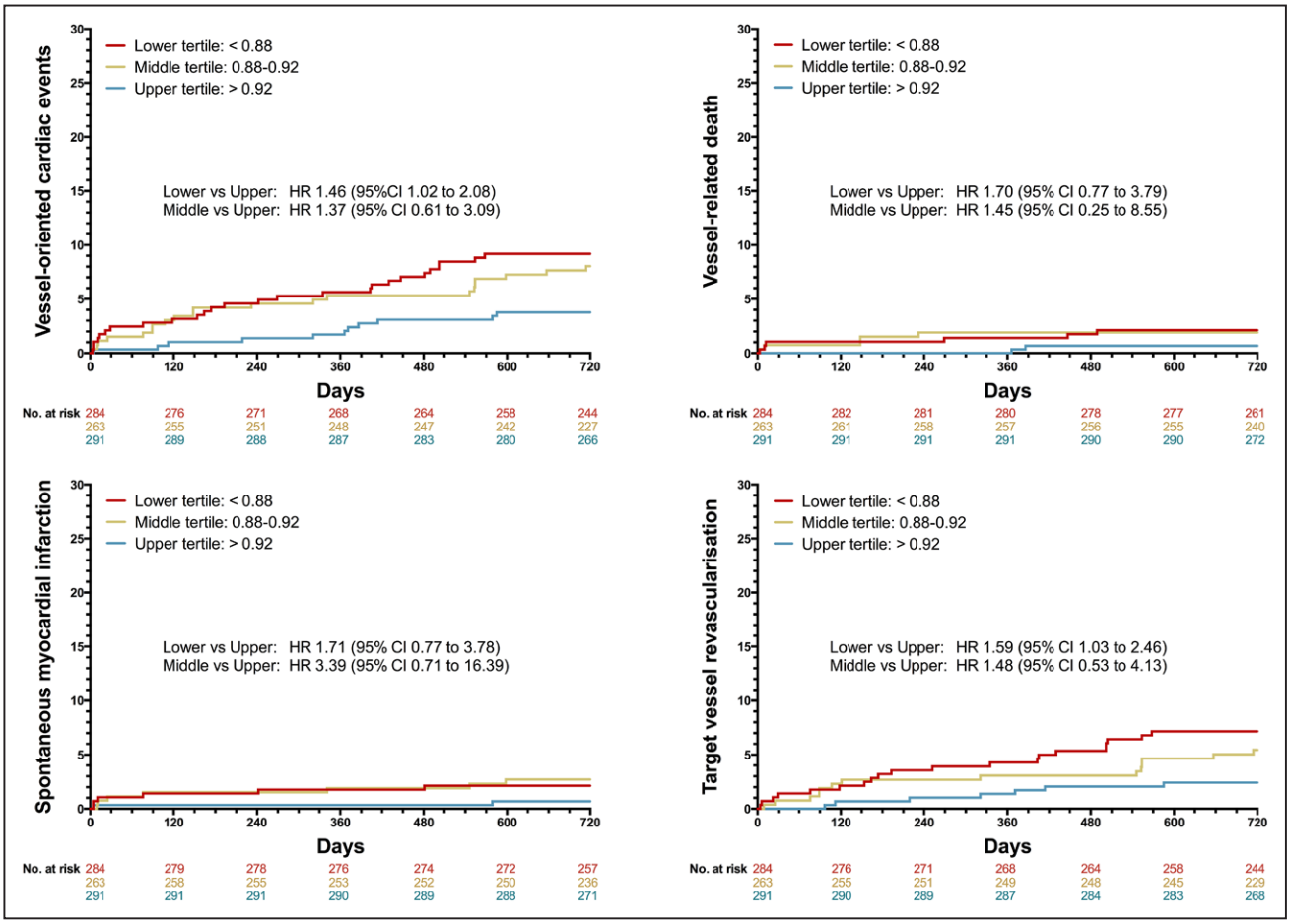

Figure 3. Two-year vessel-related event rates in lower, middle, and high post–percutaneous coronary intervention (PCI) fractional flow reserve (FFR) tertiles. In the unadjusted comparison of the 2-year outcome of the tertiles, grouped according to post-PCI FFR value, a significant difference was found in terms of overall vessel-oriented composite end point and target vessel revascularization, favoring the upper tertile. No statistically significant difference was observed in vessel-related spontaneous myocardial infarction and vessel-related cardiovascular death. CI indicates confidence interval; and HR, hazard ratio.

Table 5. Two-Year Clinical Outcome in the Tertiles According to Post-PCI FFR

	Lower (n=284)	Middle (n=263)	Upper (n=291)	HR (95% CI)	*P* Value
Unadjusted					
VOCE, n (%)	26 (9)		11 (4)	1.46 (1.02–2.08)	**0.037**
Death, n (%)	6 (2)		2 (1)	1.70 (0.77–3.79)	0.191
Spontaneous MI, n (%)	6 (2)		2 (1)	1.71 (0.77–3.78)	0.188
TVR, n (%)	20 (7)		7 (3)	1.59 (1.03–2.46)	**0.037**
Adjusted for sex, hypertension, diabetes mellitus, target vessel, serial stenosis, and baseline %DS					
VOCE, n (%)				1.40 (0.93–2.08)	0.104
Death, n (%)				1.34 (0.42–4.48)	0.602
Spontaneous MI, n (%)				1.92 (0.94–3.94)	0.074
TVR, n (%)				1.55 (0.97–2.46)	0.066
Unadjusted					
VOCE, n (%)		21 (8)	11 (4)	1.37 (0.61–3.09)	0.444
Death, n (%)		5 (2)	2 (1)	1.45 (0.25–8.55)	0.685
Spontaneous MI, n (%)		7 (3)	2 (1)	3.39 (0.71–16.39)	0.128
TVR, n (%)		14 (5)	7 (2)	1.48 (0.53–4.13)	0.460
Adjusted for sex, diabetes mellitus, target vessel, baseline %DS, and use of first-generation DES					
VOCE, n (%)				1.01 (0.45–2.28)	0.978
Death, n (%)				1.63 (0.18–14.89)	0.668
Spontaneous MI, n (%)				3.06 (0.73–12.82)	0.126
TVR, n (%)				1.17 (0.42–3.30)	0.764

Unadjusted (above) and adjusted (below) comparisons of 2-year clinical outcome of lower (<0.88) vs upper (>0.92), and middle (0.88–0.92) vs upper (>0.92) tertiles according to post-PCI FFR value. CI indicates confidence interval; DES, drug-eluting stent; %DS, percent diameter stenosis; FFR, fractional flow reserve; HR, hazard ratio; MI, myocardial infarction; TVR, target vessel revascularization; and VOCE, vessel-oriented composite end point.

post-PCI FFR achieved after angiographically successful revascularization.

3. Nevertheless, the low likelihood ratio indicates that there is no discrete post-PCI FFR value that could be proposed to rule in or to rule out vessel-oriented adverse events. Accordingly, post-PCI FFR cannot be advocated as a clinical surrogate nor as a guide for PCI optimization.

Previous Data With Post-PCI FFR

The present findings derived from the largest population studied to date confirm previous observational registries, suggesting the prognostic value of post-PCI FFR. In the bare metal stent era, a large registry showed a clear relationship between the FFR, measured immediately after PCI, and the MACE rate at 6-month follow-up.[22] In the DES era, Doh et al[23] investigated 117 lesions in 105 patients and identified a post-PCI FFR cutoff value of 0.89 as the best predictor of target vessel failure–free survival at 3 years, defined as composite of TVR, death, or nonfatal MI attributed to the target vessel. Nam et al[24] investigated 99 lesions in 80 patients and found the cutoff value of 0.91 as strongest predictor of MACE at 1 year. Other observational studies yielded conflicting results

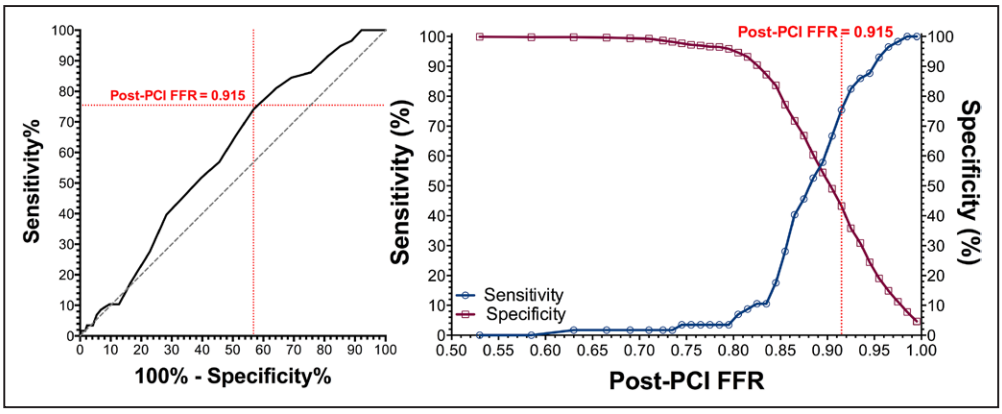

Figure 4. Definition of a potential cutoff value of post–percutaneous coronary intervention (PCI) fractional flow reserve (FFR), predicting vessel-oriented composite end point at 2-year follow-up. On the basis of receiver–operator characteristic curve analysis (**A**), a post-PCI FFR value of 0.915 was found to have the highest Youden index for predicting VOCE at 2 years, with a sensitivity of 75% and specificity of 43% (**B**).

on the ability of post-PCI FFR to predict TLR, long-term event-free survival, or restenosis.[25–28] In contrast, the present analysis was based on 2 large-scale, multicentric randomized trials. Approximately two thirds of the total population that underwent FFR-guided DES placement in these trials had post-PCI FFR measurements. Consequently, the number of patients included in the present analysis is twice as large as most of the previously published studies from the DES era together.[23–27] The end point—VOCE—was used to match as closely as possible post-PCI vessel characteristics and patients clinical outcome. Moreover, all end points were adjudicated by an independent clinical event committee blinded to all clinical data including post-PCI FFR values.

Evaluation of Post-PCI Results

In the vast majority of PCI cases, final results are gauged by angiography. A residual stenosis of >20% has often been considered a suboptimal post-PCI result.[29–31] Many of the mechanisms of early and late post-PCI failure have been unraveled by intravascular ultrasound. However, intravascular ultrasound-based guidance of PCI did not consistently translate into improved clinical outcome[32,33] and was, therefore, not adopted in clinical practice to evaluate the result of PCI. Optical coherence tomography further improved the visualization of morphological details. Even though post-PCI optical coherence tomography images often trigger additional maneuvers aiming at improving the immediate results,[34,35] there is no convincing indication that a systematic use of optical coherence tomography improves clinical outcome. An imaging modality focuses on the stented segment, not taking into account the entire length of the artery nor the myocardial mass depending on the stented segment. In contrast, post-PCI FFR is a marker of the residual epicardial resistance of the entire artery during maximal microvascular vasodilation. Several mechanisms can concur to a post-PCI FFR value <1.0: the presence of a second lesion, residual diffuse disease, pressure sensor drift, and suboptimal stent deployment.[36] Accordingly, the different mechanisms might have different weight in determining clinical outcome. A pullback maneuver of the sensor under steady-state hyperemia is able to identify which one is prevailing.[37] In case of abnormal FFR related to a pressure gradient within the stented segment, additional intracoronary imaging is warranted to unravel the mechanism of this focal pressure drop. In the patients included in the FAME trials, a pressure pull back was not performed systematically and, when done, additional maneuvers to correct and improve FFR were not advocated. However, daily experience shows that after an angiographically successful PCI, the pressure gradient is often diffusely distributed over the length of the artery caused by diffuse atherosclerosis, which may or may not be visible by angiography. FFR values measured in the present study were obtained when the PCI was considered successful and should, therefore, be considered merely documentary.

Perspectives

Our findings raise the question whether optimization of post-PCI FFR with a more extensive intervention could improve clinical outcome. An answer to this question could only be derived from an appropriately sized trial. On the basis of the present findings, such a randomized trial comparing post-PCI FFR-based optimization with routine practice would require ≈4200 patients to detect a 30% relative risk reduction of VOCE at 2 years (from 7.9% in the control group receiving routine care to 3.6% in the experimental group with 80% power at a 2-sided α of 0.05). In the light of our results, such a trial currently seems hardly justifiable.

Limitations

It is important to stress that the post-PCI values were merely documentary because, after angiographically successful PCI, according to protocol, no additional maneuver was undertaken to achieve a higher FFR value. Second, patients and their treating physicians could be aware of the post-PCI FFR value. However, all patients had angiographically successful PCI, and the vast majority had a nonsignificant FFR on completion of the intervention (Figure 1). Third, albeit measurement of post-PCI FFR was recommended in the trials, it was performed only in two thirds of all cases, suggesting some selection bias. It can indeed be speculated that post-PCI FFR measurements were preferentially performed in cases with a good angiographic result. Yet, this potential selection bias could actually only strengthen our findings. Fourth, we did not specifically investigate the effect of medical therapy and compliance of patients with the medical regimen; however, both trials mandated optimal medical therapy, and the FAME 2 trial reported on the medical therapy of different arms of the trial.[6,7] Finally, because post-PCI pullback recording during constant hyperemia was not mandated, we are unable to tell whether a suboptimal post-PCI FFR value is a result of residual diffuse coronary atherosclerosis, imperfect stenting, or pressure drift.

Clinical Implications

The higher the post-PCI FFR value, obtained immediately after DES implantation, the lower the 2-year rate of clinical events related to the stented vessel. However, the present data cannot propose a discrete post-PCI FFR cutoff value that might be used as a surrogate clinical end point or as a target value to optimize PCI results.

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References

1. Pijls NHJ, van Son JAM, Kirkeeide RL, De Bruyne B, Gould KL. Experimental basis of determining maximum coronary, myocardial, and collateral blood flow by pressure measurement for assessing functional stenosis severity before and after percutaneous transluminal coronary angioplasty. *Circulation*. 1993;86:1354–1367.
2. De Bruyne B, Baudhuin T, Melin JA, Pijls NH, Sys SU, Bol A, Paulus WJ, Heyndrickx GR, Wijns W. Coronary flow reserve calculated from pressure measurements in humans. Validation with positron emission tomography. *Circulation*. 1994;89:1013–1022.
3. Toth G, Hamilos M, Pyxaras S, Mangiacapra F, Nelis O, De Vroey F, Di Serafino L, Muller O, Van Mieghem C, Wyffels E, Heyndrickx GR, Bartunek J, Vanderheyden M, Barbato E, Wijns W, De Bruyne B. Evolving concepts of angiogram: fractional flow reserve discordances in 4000 coronary stenoses. *Eur Heart J*. 2014;35:2831–2838. doi: 10.1093/eurheartj/ehu094.
4. Bech GJ, De Bruyne B, Pijls NHJ, de Muinck ED, Hoorntje JC, Escaned J, Stella PR, Boersma E, Bartunek J, Koolen JJ, Wijns W. Fractional flow reserve to determine the appropriateness of angioplasty in moderate coronary stenosis: a randomized trial. *Circulation*. 2001;103:2928–2934.
5. Tonino PA, De Bruyne B, Pijls NH, Siebert U, Ikeno F, van' t Veer M, Klauss V, Manoharan G, Engstrøm T, Oldroyd KG, Ver Lee PN, MacCarthy PA, Fearon WF; FAME Study Investigators. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med*. 2009;360:213–224. doi: 10.1056/NEJMoa0807611.
6. De Bruyne B, Pijls NH, Kalesan B, Barbato E, Tonino PA, Piroth Z, Jagic N, Möbius-Winkler S, Mobius-Winckler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engström T, Oldroyd KG, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Jüni P, Fearon WF; FAME 2 Trial Investigators. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med*. 2012;367:991–1001. doi: 10.1056/NEJMoa1205361.
7. De Bruyne B, Fearon WF, Pijls NH, Barbato E, Tonino P, Piroth Z, Jagic N, Mobius-Winckler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engström T, Oldroyd K, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Limacher A, Nüesch E, Jüni P; FAME 2 Trial Investigators. Fractional flow reserve-guided PCI for stable coronary artery disease. *N Engl J Med*. 2014;371:1208–1217. doi: 10.1056/NEJMoa1408758.
8. Zimmermann FM, Ferrara A, Johnson NP, van Nunen LX, Escaned J, Albertsson P, Erbel R, Legrand V, Gwon HC, Remkes WS, Stella PR, van Schaardenburgh P, Bech GJ, De Bruyne B, Pijls NH. Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial. *Eur Heart J*. 2015;36:3182–3188. doi: 10.1093/eurheartj/ehv452.
9. van Nunen LX, Zimmermann FM, Tonino PA, Barbato E, Baumbach A, Engstrøm T, Klauss V, MacCarthy PA, Manoharan G, Oldroyd KG, Ver Lee PN, Van't Veer M, Fearon WF, De Bruyne B, Pijls NH; FAME Study Investigators. 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;386:1853–1860. doi: 10.1016/S0140-6736(15)00057-4.
10. Tonino PA, Fearon WF, De Bruyne B, Oldroyd KG, Leesar MA, Ver Lee PN, Maccarthy PA, Van't Veer M, Pijls NH. Angiographic versus functional severity of coronary artery stenoses in the FAME study fractional flow reserve versus angiography in multivessel evaluation. *J Am Coll Cardiol*. 2010;55:2816–2821. doi: 10.1016/j.jacc.2009.11.096.
11. De Bruyne B, Pijls NH, Bartunek J, Kulecki K, Bech JW, De Winter H, Van Crombrugge P, Heyndrickx GR, Wijns W. Fractional flow reserve in patients with prior myocardial infarction. *Circulation*. 2001;104:157–162.
12. Hamilos M, Muller O, Cuisset T, Ntalianis A, Chlouverakis G, Sarno G, Nelis O, Bartunek J, Vanderheyden M, Wyffels E, Barbato E, Heyndrickx GR, Wijns W, De Bruyne B. Long-term clinical outcome after fractional flow reserve-guided treatment in patients with angiographically equivocal left main coronary artery stenosis. *Circulation*. 2009;120:1505–1512. doi: 10.1161/CIRCULATIONAHA.109.850073.
13. Muller O, Mangiacapra F, Ntalianis A, Verhamme KM, Trana C, Hamilos M, Bartunek J, Vanderheyden M, Wyffels E, Heyndrickx GR, van Rooij FJ, Witteman JC, Hofman A, Wijns W, Barbato E, De Bruyne B. Long-term follow-up after fractional flow reserve-guided treatment strategy in patients with an isolated proximal left anterior descending coronary artery stenosis. *JACC Cardiovasc Interv*. 2011;4:1175–1182. doi: 10.1016/j.jcin.2011.09.007.
14. Puymirat E, Peace A, Mangiacapra F, Conte M, Ntarladimas Y, Bartunek J, Vanderheyden M, Wijns W, De Bruyne B, Barbato E. Long-term clinical outcome after fractional flow reserve-guided percutaneous coronary revascularization in patients with small-vessel disease. *Circ Cardiovasc Interv*. 2012;5:62–68. doi: 10.1161/CIRCINTERVENTIONS.111.966937.
15. Di Serafino L, De Bruyne B, Mangiacapra F, Bartunek J, Agostoni P, Vanderheyden M, Scognamiglio G, Heyndrickx GR, Wijns W, Barbato E. Long-term clinical outcome after fractional flow reserve- versus angio-guided percutaneous coronary intervention in patients with intermediate stenosis of coronary artery bypass grafts. *Am Heart J*. 2013;166:110–118. doi: 10.1016/j.ahj.2013.04.007.
16. Toth G, De Bruyne B, Casselman F, De Vroey F, Pyxaras S, Di Serafino L, Van Praet F, Van Mieghem C, Stockman B, Wijns W, Degrieck I, Barbato E. Fractional flow reserve-guided versus angiography-guided coronary artery bypass graft surgery. *Circulation*. 2013;128:1405–1411. doi: 10.1161/CIRCULATIONAHA.113.002740.
17. Pijls NH, Fearon WF, Tonino PA, Siebert U, Ikeno F, Bornschein B, van't Veer M, Klauss V, Manoharan G, Engstrøm T, Oldroyd KG, Ver Lee PN, MacCarthy PA, De Bruyne B; FAME Study Investigators. 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;56:177–184. doi: 10.1016/j.jacc.2010.04.012.
18. Johnson NP, Tóth GG, Lai D, Zhu H, Açar G, Agostoni P, Appelman Y, Arslan F, Barbato E, Chen SL, Di Serafino L, Domínguez-Franco AJ, Dupouy P, Esen AM, Esen OB, Hamilos M, Iwasaki K, Jensen LO, Jiménez-Navarro MF, Katritsis DG, Kocaman SA, Koo BK, López-Palop R, Lorin JD, Miller LH, Muller O, Nam CW, Oud N, Puymirat E, Rieber J, Rioufol G, Rodés-Cabau J, Sedlis SP, Takeishi Y, Tonino PA, Van Belle E, Verna E, Werner GS, Fearon WF, Pijls NH, De Bruyne B, Gould KL. Prognostic value of fractional flow reserve: linking physiologic severity to clinical outcomes. *J Am Coll Cardiol*. 2014;64:1641–1654. doi: 10.1016/j.jacc.2014.07.973.
19. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Jüni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A. 2014 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J*. 2014;35:2541–2619.
20. Barbato E, Toth GG, Johnson NP, Pijls NH, Fearon WF, Tonino PA, Curzen N, Piroth Z, Rioufol G, Jüni P, De Bruyne B. A prospective natural history study of coronary atherosclerosis using fractional flow reserve. *J Am Coll Cardiol*. 2016;68:2247–2255. doi: 10.1016/j.jacc.2016.08.055.
21. Pencina MJ, D'Agostino RB Sr, D'Agostino RB Jr, Vasan RS. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. *Stat Med*. 2008;27:157–72; discussion 207. doi: 10.1002/sim.2929.
22. Pijls NH, Klauss V, Siebert U, Powers E, Takazawa K, Fearon WF, Escaned J, Tsurumi Y, Akasaka T, Samady H, De Bruyne B; Fractional Flow Reserve (FFR) Post-Stent Registry Investigators. Coronary pressure measurement after stenting predicts adverse events at follow-up: a multicenter registry. *Circulation*. 2002;105:2950–2954.
23. Doh JH, Nam CW, Koo BK, Lee SY, Choi H, Namgung J, Kwon SU, Kwak JJ, Kim HY, Choi WH, Lee WR. Clinical relevance of poststent fractional flow reserve after drug-eluting stent implantation. *J Invasive Cardiol*. 2015;27:346–351.
24. Nam CW, Hur SH, Cho YK, Park HS, Yoon HJ, Kim H, Chung IS, Kim YN, Kim KB, Doh JH, Koo BK, Tahk SJ, Fearon WF. Relation of fractional flow reserve after drug-eluting stent implantation to one-year outcomes. *Am J Cardiol*. 2011;107:1763–1767. doi: 10.1016/j.amjcard.2011.02.329.
25. Matsuo A, Fujita H, Tanigaki T, Shimonaga T, Ueoka A, Tsubakimoto Y, Sakatani T, Kimura S, Inoue K, Kitamura M. Clinical implications of coronary pressure measurement after stent implantation. *Cardiovasc Interv Ther*. 2013;28:170–177. doi: 10.1007/s12928-012-0147-7.

26. Leesar MA, Satran A, Yalamanchili V, Helmy T, Abdul-Waheed M, Wongpraparut N. The impact of fractional flow reserve measurement on clinical outcomes after transradial coronary stenting. *EuroIntervention*. 2011;7:917–923. doi: 10.4244/EIJV7I8A145.
27. Ishii H, Kataoka T, Kobayashi Y, Tsumori T, Takeshita H, Matsumoto R, Shirai N, Nishioka H, Hasegawa T, Nakata S, Shimada Y, Ehara S, Muro T, Yoshiyama M. Utility of myocardial fractional flow reserve for prediction of restenosis following sirolimus-eluting stent implantation. *Heart Vessels*. 2011;26:572–581. doi: 10.1007/s00380-010-0105-1.
28. Agarwal SK, Kasula S, Hacioglu Y, Ahmed Z, Uretsky BF, Hakeem A. Utilizing post-intervention fractional flow reserve to optimize acute results and the relationship to long-term outcomes. *JACC Cardiovasc Interv*. 2016;9:1022–1031. doi: 10.1016/j.jcin.2016.01.046.
29. Leon MB, Baim DS, Popma JJ, Gordon PC, Cutlip DE, Ho KK, Giambartolomei A, Diver DJ, Lasorda DM, Williams DO, Pocock SJ, Kuntz RE. A clinical trial comparing three antithrombotic-drug regimens after coronary-artery stenting. Stent Anticoagulation Restenosis Study Investigators. *N Engl J Med*. 1998;339:1665–1671. doi: 10.1056/NEJM199812033392303.
30. Di Mario C, Moses JW, Anderson TJ, Bonan R, Muramatsu T, Jain AC, Suarez de Lezo J, Cho SY, Kern M, Meredith IT, Cohen D, Moussa I, Colombo A. Randomized comparison of elective stent implantation and coronary balloon angioplasty guided by online quantitative angiography and intracoronary Doppler. DESTINI Study Group (Doppler Endpoint STenting INternational Investigation). *Circulation*. 2000;102:2938–2944.
31. Serruys PW, de Bruyne B, Carlier S, Sousa JE, Piek J, Muramatsu T, Vrints C, Probst P, Seabra-Gomes R, Simpson I, Voudris V, Gurné O, Pijls N, Belardi J, van Es GA, Boersma E, Morel MA, van Hout B. Randomized comparison of primary stenting and provisional balloon angioplasty guided by flow velocity measurement. Doppler Endpoints Balloon Angioplasty Trial Europe (DEBATE) II Study Group. *Circulation*. 2000;102:2930–2937.
32. Zhang Y, Farooq V, Garcia-Garcia HM, Bourantas CV, Tian N, Dong S, Li M, Yang S, Serruys PW, Chen SL. Comparison of intravascular ultrasound versus angiography-guided drug-eluting stent implantation: a meta-analysis of one randomised trial and ten observational studies involving 19,619 patients. *EuroIntervention*. 2012;8:855–865. doi: 10.4244/EIJV8I7A129.
33. Parise H, Maehara A, Stone GW, Leon MB, Mintz GS. Meta-analysis of randomized studies comparing intravascular ultrasound versus angiographic guidance of percutaneous coronary intervention in pre-drug-eluting stent era. *Am J Cardiol*. 2011;107:374–382. doi: 10.1016/j.amjcard.2010.09.030.
34. Wijns W, Shite J, Jones MR, Lee SW, Price MJ, Fabbiocchi F, Barbato E, Akasaka T, Bezerra H, Holmes D. Optical coherence tomography imaging during percutaneous coronary intervention impacts physician decision-making: ILUMIEN I study. *Eur Heart J*. 2015;36:3346–3355. doi: 10.1093/eurheartj/ehv367.
35. Meneveau N, Souteyrand G, Motreff P, Caussin C, Amabile N, Ohlmann P, Morel O, Lefrançois Y, Descotes-Genon V, Silvain J, Braik N, Chopard R, Chatot M, Ecarnot F, Tauzin H, Van Belle E, Belle L, Schiele F. Optical coherence tomography to optimize results of percutaneous coronary intervention in patients with non-ST-elevation acute coronary syndrome: results of the multicenter, randomized DOCTORS study (Does Optical Coherence Tomography Optimize Results of Stenting). *Circulation*. 2016;134:906–917. doi: 10.1161/CIRCULATIONAHA.116.024393.
36. Toth GG, Johnson NP, Jeremias A, Pellicano M, Vranckx P, Fearon WF, Barbato E, Kern MJ, Pijls NH, De Bruyne B. Standardization of fractional flow reserve measurements. *J Am Coll Cardiol*. 2016;68:742–753. doi: 10.1016/j.jacc.2016.05.067.
37. Tonino PA, Johnson NP. Why is fractional flow reserve after percutaneous coronary intervention not always 1.0? *JACC Cardiovasc Interv*. 2016;9:1032–1035. doi: 10.1016/j.jcin.2016.04.001.