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The prognostic value of angiography-based vessel fractional flow reserve after percutaneous coronary intervention: The FAST Outcome study

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ABSTRACT

Background: Vessel Fractional Flow Reserve (vFFR) as assessed by three-dimensional quantitative coronary angiography has high correlation with pressure wire-based fractional flow reserve in both a pre- and post-PCI setting. The present study aims to assess the prognostic value of post-PCI vFFR on the incidence of target vessel failure (TVF), a composite endpoint of cardiac death, target vessel myocardial infarction and target vessel revascularization (TVR) at 5-year follow up.

Methods: Post-PCI vFFR was calculated after routine PCI in a total of 748 patients (832 vessels) with available orthogonal angiographic projections of the stented segment.

Results: Median age was 65 (IQR 55–74) years, 18.2% were diabetic, and 29.1% presented with stable angina. Median post-PCI vFFR was 0.91 (IQR 0.86–0.95). Vessels were categorized into tertiles based on post-PCI vFFR: low (vFFR <0.88), middle (vFFR 0.88–0.93), and upper (vFFR ≥0.94). Vessels in the lower and middle tertile were more often LADs and had smaller stent diameters ($p<0.001$). Vessels in the lower and middle tertile had a higher risk of TVF as compared to vessels in the upper tertile (24.6% and 21.5% vs. 17.1%; adjusted HR 1.84 (95%CI 1.15–2.95), $p = 0.011$, and 1.58 (95%CI 1.02–2.45), $p = 0.040$) at 5-years follow-up. Additionally, vessels in the lower tertile had higher rates of TVR as compared to vessels in the higher tertile (12.6% vs. 6.5%, adjusted HR 1.93 (95%CI 1.06–3.53), $p = 0.033$).

Conclusion: Lower post-PCI vFFR values are associated with a significantly increased risk of TVF and TVR at 5-years follow-up.

1. Introduction

Both fractional flow reserve (FFR) and non-hyperemic pressure ratios (NHPR) are widely used to assess the hemodynamic importance of intermediate coronary artery lesions [1–4]. While the specific merits of each of these physiological indices have been mainly validated in a pre-percutaneous coronary intervention (PCI) setting, there is increasing interest in the use of either FFR or NHPR to assess the direct impact of stent placement on post-PCI physiology. The importance of the latter was demonstrated by several studies showing that despite optimal angiographic results, post-PCI FFR remained suboptimal in up to 40% of patients and resulted in a significantly increased risk for future major adverse cardiac events [5–10].

Recently, as an alternative to the abovementioned wire based pressure ratios, several 3-Dimensional Quantitative Coronary Angiography (3D-QCA) based FFR indices have been validated as easier approaches to assess coronary physiology. As such, vessel FFR (vFFR) strongly correlates to conventional invasive FFR, both in a pre- and post-PCI setting [11,12]. The evolution of this non-invasive technology may increase the uptake of post-PCI physiological assessment to identify those patients at the highest risk of target vessel failure (TVF).

The present study aims to assess the prognostic value of post-PCI vFFR on the incidence of TVF at long-term follow-up up to 5-years.

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2. Methods

2.1. Study design and population

The FAST Outcome study is a retrospective cohort study in which patients were recruited from the P-SEARCH registry – a single-center, prospective all-comer cohort study comparing 1-year clinical outcome data of patients treated with either everolimus-eluting platinum-chromium stents (Promus Premier™, Boston Scientific, Natick, Massachusetts) or everolimus-eluting cobalt-chromium stents (Xience Prime™, Abbott Vascular, Santa Clara, California) between 2012 and 2014 ($N = 2000$) [13]. The present study aimed to assess the prognostic value of post-PCI vFFR on the incidence of TVF, a composite endpoint of cardiovascular death, spontaneous target vessel myocardial infarction (TVMI) and target vessel revascularization (TVR) at 5 years follow-up. The Institutional Review Board of the Erasmus Medical University Center waived ethical approval for the FAST Outcome due to the retrospective nature of the data used.

Patients ≥18 years of age who underwent PCI in at least one native coronary artery were eligible for the present study. Exclusion criteria were: arterial or saphenous vein bypass grafts to the target vessel, cardiogenic shock or severe hemodynamic instability, history of cardiac allograft transplantation and congenital heart disease. In addition, two sufficient orthogonal angiographic projections post-stenting needed to be available with minimal overlap and foreshortening to facilitate vFFR analysis.

2.2. PCI procedure

Patients underwent PCI with second generation drug-eluting stents according to local routine clinical practice. During each procedure invasive aortic root pressure was continuously recorded and stored. Final angiographic projections were made at the operators discretion and were not protocol-mandated. DICOM images, hemodynamic data and pressure waveform data were stored for offline analyses for all cases in a dedicated database.

2.3. Computation of vFFR

Post-PCI vFFR was calculated using the final two orthogonal angiographic projections of the vessel that was stented. Computation of vFFR was performed offline by trained analysts (TN, AS) using validated software (CAAS Workstation 8.2, Pie Medical Imaging, Maastricht, the Netherlands) [11].

The software requires two orthogonal angiographic projections (at least 30 degrees in rotation and/or angulation) without vessel overlap or foreshortening and the invasively measured aortic root pressure to model a 3D-reconstruction and the pressure drop along the whole coronary artery. For this analysis, we used the last available aortic root pressure prior to the acquisition of the final coronary angiograms. The software is able to automatically identify end-diastolic frames, and contour detection is performed semi-automatically. In case of suboptimal automatic contour detection manual correction was allowed. For the calculation of the post-PCI vFFR values in the present study, the vessel contour was delineated in the two final angiographic films from the ostium to the distal coronary artery. The distal measurement site was taken at least 20 mm distal from the distal stent edge, and until the vessel diameter was <2.25 mm.

2.4. Endpoint definitions and clinical follow up

The primary endpoint of TVF was a composite of cardiovascular death, TVMI or TVR at 5 year follow-up. Secondary endpoints were the individual endpoints of the composite endpoint, target vessel (TV) stent thrombosis, and all-cause mortality. All endpoints were defined in accordance with the Academic Research Consortium-2 Consensus Document [14]. Death of unknown cause was considered to be cardiovascular death. Event adjudication was performed by trained study personnel blinded to the post-PCI vFFR values.

Clinical follow-up data were obtained from hospital electronic medical records and health questionnaires sent to all living patients requesting for patient reported outcome measurements. All patient reported events were verified with source documentation. Survival data were obtained through a municipal civil registry check.

2.5. Statistical analysis

Continuous variables are presented as medians with interquartile ranges (IQR) since all had a non-normal distribution (according to the Shapiro-Wilk test). Categorical variables are reported as counts and percentages. As no cut-offs for post-PCI vFFR have been proposed yet, we grouped the post-PCI vFFR values into tertiles on a vessel-level, in line with previous reports on post-PCI FFR [9,10]. Patients were grouped into tertiles according to their lowest post-PCI vFFR value. To test for differences among the tertiles, patient-level variables were analyzed using the Kruskal-Wallis test (continuous variables) and the chi-square trend test (categorical variables). For vessel-level variables, (generalized) linear mixed effect models were built with post-PCI vFFR tertile as the independent variable, and the variable of interest as dependent variables, and random intercepts per individual patient to take into account clustering of vessels in patients.

Additionally, in line with previous studies on the topic we performed receiver operator characteristic (ROC) curve analysis to evaluate the discriminative ability and to derive the optimal cut-off value (determined as maximization of the Youden index) of post-PCI vFFR to predict 5-year TVF [8,9,15–18].

Patients were followed-up until they experienced the event of interest, or until censoring at the moment that they were lost-to-follow-up or had completed 5-year follow-up (1825 days). The cumulative incidence function was used to derive cumulative event rates at 5-years follow-up. Univariate and multivariate cox proportional hazard regression models with robust standard errors (to correct for clustering of vessels in patients) were built to provide effect estimates and to correct for confounders and other influential factors. Schoenfeld residual tests were performed for all models under evaluation to check the proportional hazard assumption: in case of violation, stratification was performed. Covariates for the multivariate cox regression models were chosen based on the literature and their univariate association with the endpoint of interest (age and gender were always included). To avoid overfitting, a maximum of 1 degree of freedom per 10 events was used in the cox regression models for the events of interest.

Given uncertainties regarding the validity of post-PCI physiology in the presence of ST-elevation myocardial infarction (STEMI), we also performed additional sub-analyses excluding all patients that presented with STEMI.

All tests were two-tailed and a p-value <0.05 was considered as statistically significant. Statistical analyses were performed by IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA) and R (R Core Team 2019; version 3.5.2, packages: cmprsk, survival, lme4, nlme).

3. Results

3.1. Patients and vessels demographics

Of the 2000 patients included in the P-Search registry, a total of 748 patients including 832 treated coronary arteries fulfilled inclusion and exclusion criteria for the FAST OUTCOME study (Fig. S1).

Baseline patient and procedural characteristics are depicted in Table 1. Median age was 65 (IQR 55–74) years, 70.3% of patients were male, and diabetes mellitus was present in 18.2% of patients. A total of 29.1% of patients presented with stable angina. PCI was guided by

Table 1
Baseline patient- and vessel-level variables according to post-PCI vFFR tertiles. Data is presented as medians (interquartile ranges) or counts and percentages.

Patient-level variables	All *N* = 748	Lower tertile vFFR < 0.88 *N* = 253	Middle tertile vFFR 0.88–0.93 *N* = 257	Upper tertile vFFR ≥ 0.94 *N* = 238	*P*-value for trend
Age, in years	65 (55–74)	65 (56–73)	65 (54–75)	64 (55–73)	0.92
Male gender	526 (70.3%)	181 (71.5%)	172 (66.9%)	173 (72.7%)	0.80
Clinical presentation					0.022
Stable angina	218 (29.1%)	80 (31.6%)	80 (31.1%)	58 (24.4%)	
NSTE-ACS	297 (39.7%)	105 (41.5%)	97 (37.7%)	95 (39.9%)	
STEMI	233 (31.1%)	68 (26.9%)	80 (31.1%)	85 (35.7%)	
Cardiovascular risk factors					
Hypertension	397 (53.1%)	139 (54.9%)	130 (50.6%)	128 (53.8%)	0.78
Hypercholesterolemia	314 (42.0%)	114 (45.1%)	116 (45.1%)	84 (35.3%)	0.030
Diabetes mellitus	136 (18.2%)	53 (20.9%)	38 (14.8%)	45 (18.9%)	0.54
Current smoker	218 (29.1%)	63 (24.9%)	76 (29.6%)	79 (33.2%)	0.043
Cardiovascular history					
Peripheral arterial disease	52 (7.0%)	20 (7.9%)	14 (5.4%)	18 (7.6%)	0.87
Prior myocardial infarction	150 (20.1%)	49 (19.4%)	46 (17.9%)	55 (23.1%)	0.31
Prior PCI	193 (25.8%)	68 (26.9%)	64 (24.9%)	61 (25.6%)	0.75
Prior CABG	24 (3.2%)	6 (2.4%)	10 (3.9%)	8 (3.4%)	0.53

Vessel-level variables	All *N* = 832	Lower tertile vFFR < 0.88 *n* = 262	Middle tertile vFFR 0.88–0.93 *n* = 288	Upper tertile vFFR ≥ 0.94 *n* = 282	P-value for trend*
Post-PCI vFFR	0.91 (0.86–0.95)	0.84 (0.80–0.86)	0.90 (0.89–0.92)	0.97 (0.95–0.98)	n/a
Target vessel LAD	356 (42.8%)	183 (69.8%)	160 (55.6%)	13 (4.6%)	<0.001
Bifurcation treatment	79 (9.5%)	28 (10.7%)	27 (9.4%)	24 (8.5%)	0.36
Calcification	186 (22.4%)	56 (21.4%)	75 (26.0%)	55 (19.5%)	0.19
In-stent restenosis	49 (5.9%)	15 (5.7%)	15 (5.2%)	19 (6.7%)	0.54
Thrombus	204 (24.5%)	54 (20.6%)	74 (25.7%)	76 (27.0%)	0.037
Ostial lesion	71 (8.5%)	26 (9.9%)	22 (7.6%)	23 (8.2%)	0.38
Lesion type B2/C	583 (70.1%)	192 (73.3%)	191 (66.3%)	200 (70.9%)	0.50
Nr. of stents	1 (1–2)	1 (1–2)	1 (1–2)	1 (1–2)	0.44
Total stent length in mm	23 (16–38)	24 (16–38)	23 (16–35)	24 (16–38)	0.66
Average stent diameter in mm	3.00 (2.75–3.50)	3.00 (2.67–3.09)	3.00 (2.75–3.50)	3.50 (3.00–3.50)	<0.001
Predilatation	476 (57.2%)	157 (59.9%)	166 (57.6%)	153 (54.3%)	0.19
Postdilatation	235 (28.2%)	78 (29.8%)	80 (27.8%)	77 (27.3%)	0.42

CABG indicates coronary artery bypass grafting; LAD, left anterior descending; NSTE-ACS, non-ST elevation acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; vFFR, vessel fractional flow reserve.
* *P*-values for trend for vessel-level variables were obtained from mixed models with post-PCI vFFR tertile (independent variable) as a continuous variable.

intravascular imaging in 13.6% of patients.

The left anterior descending (LAD) was the vessel of interest in 42.8% of the analyses. Median post-PCI vFFR was 0.91 (IQR 0.86–0.95), and post-PCI vFFR ranged from 0.50 to 1.03 (Fig. 1). Post-PCI vFFR was ischemic (≤0.80) in 74 vessels (8.9%).

When grouped into tertiles (lower tertile: post-PCI vFFR <0.88, middle tertile: post-PCI FFR 0.88–0.93, and upper tertile: post-PCI vFFR ≥0.94), we observed that patients with higher post-PCI vFFR values more often presented with ST-elevation myocardial infarction, and were more often current smokers, whereas hypercholesterolemia was less common in these patients (p for trend: <0.05). Conversely, in vessels with lower post-PCI vFFR values, the LAD was more often the vessel of interest (lower tertile, 69.8%; middle tertile, 55.6%; upper tertile, 4.6%, p for trend <0.001), and average stent diameters were smaller (lower tertile, 3.00 (2.67–3.09)mm; middle tertile, 3.00(2.75–3.50)mm; upper tertile, 3.50(3.00–3.50)mm, p for trend <0.001). Lesions located in vessels with higher post-PCI vFFR values were more often thrombotic (upper tertile: 27.0% vs. 20.6% and 25.7% in the lower and middle tertile, respectively, *p* for trend 0.037).

3.2. Clinical outcomes at 5-years follow up

Median total follow-up time was 5.0 (IQR 3.6–5.0) years. At 5-year follow-up, a total of 163 (21.0%) TVF events had occurred. TVF

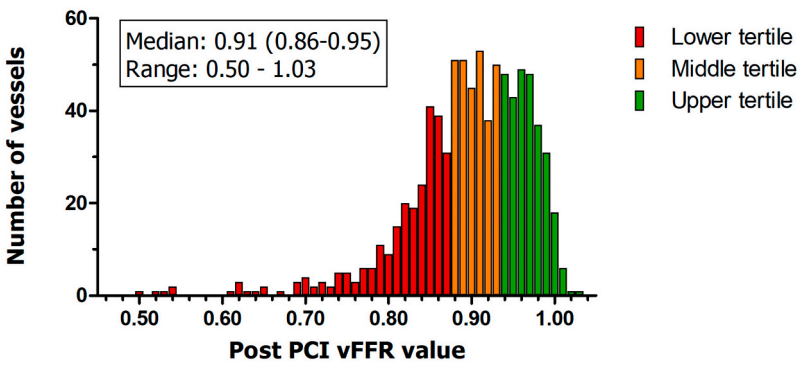

Fig. 1. Frequency distribution of post-PCI vFFR values.
PCI indicates percutaneous coronary intervention; vFFR, vessel fractional flow reserve.

occurred in 60 (24.0%) vessels in the lower tertile vs. 45 (17.1%) in the upper tertile (HR 1.53 (95% CI 1.04–2.25), $p = 0.030$) (Table 2, Fig. 2). After multivariate adjustment, vessels with post-PCI vFFR in the lower tertile had a 1.8 fold increase in the risk of TVF at 5-years follow-up (adjusted HR 1.84 (95% CI 1.15–2.95), $p = 0.011$). The increased rate of TVF in vessels within the lower tertile was mainly driven by the occurrence of TVR: a total of 30 vessels (12.6%) in the lower tertile experienced TVR at 5-year follow-up, whereas only 17 vessels (6.5%) with a post-PCI vFFR in the upper tertile had a TVR event at 5-year follow-up (HR 2.05 (95% CI 1.12–3.75), $p = 0.020$), which remained significant after multivariate adjustment (adjusted HR 1.93 (95% CI 1.06–3.53), $p = 0.033$). Vessels in the middle tertile also had a significant higher rate of TVF at 5-year follow-up as compared to the upper tertile after multivariate adjustment (adjusted HR 1.58 (95% CI 1.02–2.45), $p = 0.040$), and a tendency towards higher TVR in the middle tertile as compared to the upper tertile was observed (adjusted HR 1.68 (95% CI 0.93–3.03), $p = 0.085$). Incidences of cardiovascular death (12.7%), TVMI (3.9%), TV-Stent Thrombosis (0.9%), and all-cause mortality (19.1%) at 5-year follow-up were comparable among the tertiles. The findings were consistent in a sub-analysis excluding vessels of patients presenting with ST-segment elevation myocardial infarction (Table S1).

ROC curve analysis was performed to identify an optimal cut-off of post-PCI vFFR to predict 5-year TVF, and revealed poor discrimination (AUC 0.54, 95% CI 0.49–0.59, $p = 0.11$) of post-PCI vFFR to predict TVF at 5 year follow-up (Fig. S2).

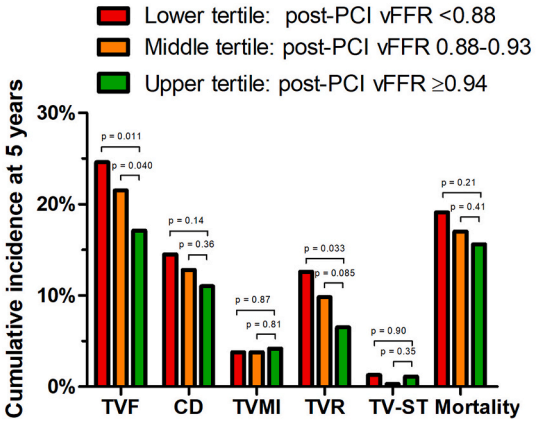

Fig. 2. Cumulative incidence rates for the events at 5-year follow-up.
The red (left-side) bars denote the cumulative event rates (in percentages) of vessels with post-PCI vFFR <0.88 (lower tertile), the orange (middle) bars represent the cumulative event rates of vessels with post-PCI vFFR between 0.88 and 0.93 (middle tertile), and the green (right-side) bars show the cumulative event rates for patients with vFFR ≥0.94 (upper tertile).
CD indicates cardiac death; TVF, target vessel failure; TVMI, target vessel myocardial infarction; TVR, target vessel revascularization; TV-ST, target vessel stent thrombosis; vFFR, vessel fractional flow reserve. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

4. Discussion

The FAST Outcome study investigated the prognostic value of post-PCI vFFR on long-term vessel-related events. The findings of the FAST Outcome study can be summarized as follows: 1) Vessels with lower post-PCI vFFR values are more often located in the LAD and have smaller average stent diameters; 2) Vessels with lower post-PCI vFFR values are at increased risk of TVF and TVR at 5-year follow-up.

Suboptimal post-PCI FFR is present in up to 40% of vessels and is related to an increased risk for future adverse cardiovascular events [5–10]. In the DEFINE PCI study, post-PCI instantaneous wave-free ratio (iFR) was ≤0.89 in 22% of vessels, and a post-PCI iFR <0.95 proved to be an independent predictor of cardiac death and myocardial infarction at 1-year follow-up [18,19]. With respect to angiography-based indices, post-PCI quantitative flow ratio (QFR, QAngio XA 3D, Medis, Medical Imaging System), both as a continuous and binary value (≤0.89), was related to a significantly increased risk of vessel-oriented composite endpoint (VOCE; vessel related cardiac death, vessel-related myocardial infarction, and target vessel revascularization) at 2 years [16]. These findings were replicated in a post-hoc derived analysis from the SYNTAX II trial, where a post-PCI QFR <0.91 was found to be a predictor of 2-year VOCE [17].

To the best of our knowledge, the present study is the first to correlate post-PCI vFFR to long-term cardiovascular events. We found a linear association between post-PCI vFFR and clinical outcome, supporting the concept of using post-PCI (angiography-based) physiology as a tool to predict future adverse events. Despite the superiority of physiology as compared to angiography-guided PCI, the uptake of the various physiological measurement tools and indices in real world practice, especially in a post-PCI setting, is still limited [20,21]. The latter has been linked to the need for costly pressure wires or microcatheters, procedural time, issues with drift, and hyperemic agents with known side effects. While the issues of cost and time were refuted in future dedicated studies, the introduction of vFFR, being an easy to use non-invasive diagnostic tool, may eventually lead to focused post-PCI optimization in selected cases. However, it remains to be determined

Table 2
Five-year follow-up outcomes for vessels according to tertiles.

	Number of events at 5-year			Lower vs upper tertile				Middle vs upper tertile			
Event of interest	Lower tertile N = 262	Middle tertile N = 288	Upper tertile N = 282	HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value	HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
TVF	60 (24.6%)	58 (21.5%)	45 (17.1%)	1.53 (1.04–2.25)	0.030	1.84 (1.15–2.95)	0.011	1.33 (0.92–1.92)	0.13	1.58 (1.02–2.45)	0.040
Cardiovascular death	35 (14.5%)	34 (12.8%)	29 (11.0%)	1.34 (0.82–2.17)	0.24	1.45 (0.88–2.39)	0.14	1.18 (0.74–1.88)	0.48	1.24 (0.78–1.96)	0.36
TVMI	9 (3.8%)	10 (3.8%)	11 (4.2%)	0.91 (0.38–2.18)	0.83	0.93 (0.38–2.24)	0.87	0.92 (0.39–2.18)	0.86	0.90 (0.38–2.13)	0.81
TVR	30 (12.6%)	26 (9.8%)	17 (6.5%)	2.05 (1.12–3.75)	0.020	1.93 (1.06–3.53)	0.033	1.59 (0.88–2.85)	0.12	1.68 (0.93–3.03)	0.085
TV Stent thrombosis	3 (1.3%)	1 (0.3%)	3 (1.1%)	1.11 (0.23–5.50)	0.90	n/a*	n/a*	0.34 (0.04–3.23)	0.35	n/a*	n/a*
All-cause mortality	46 (19.1%)	45 (17.0%)	41 (15.6%)	1.25 (0.82–1.88)	0.30	1.32 (0.86–2.02)	0.21	1.11 (0.74–1.65)	0.62	1.19 (0.79–1.79)	0.41

HR indicates hazard ratio; TVF, target vessel failure; TVMI, target vessel myocardial infarction; TVR, target vessel revascularization; TV, target vessel; vFFR, vessel fractional flow reserve.
* No multivariate models built due to limited number of events.

into what format post-PCI physiology might warrant further assessment, treatment or follow-up. Dedicated trials aimed to evaluate whether functional PCI optimization based on unsatisfactory post-PCI values of physiological indices improves patient outcome are currently awaited (DEFINE GPS: NCT04451044 and the FFR REACT trial: NL6523).

In patients with suboptimal post-PCI physiology, a special role may be reserved for intravascular imaging. Up to 84% of patients with post-PCI FFR ≤0.85 proved to have significant residual disease, when analyzed using intravascular ultrasound, findings that went unnoticed by routine coronary angiography evaluation [22]. Intravascular imaging might therefore have an important role in focused PCI optimization. Additionally, how local physiological pressure drops (proximal, in-stent or distal to the stent), being either pressure wire- or 3D-QCA based, correspond to intravascular imaging findings, and whether they also have to ability to direct PCI optimization, remains subject of future studies.

When scrutinizing the rationale for differences in patient characteristics between the tertiles, we found that patients with the highest post-PCI vFFR values more often presented with STEMI, and, consistently, more often had thrombus containing lesions. Although the latter is consistent with previous data based on conventional pressure wire-based FFR, concerns regarding the validity of hyperemic flow and higher microvascular resistance in the setting of STEMI cannot be extended to angiography-derived physiological indices based on computational fluid dynamics. A potential reason for the higher percentage of STEMI patients in the highest post-PCI vFFR tertile could be that these patients had less diffuse disease along with the larger average stent diameters found in patients with the highest post-PCI vFFR values.

Moreover, we observed that stents located in the LAD exhibited lower post-PCI vFFR values as compared to non-LAD vessels. Although consistent with previous pressure wire-based FFR studies, in which this phenomenon was hypothesized to be linked to larger myocardial territories and an increased coronary flow in the LAD, also this concept does not apply to angiography-based indices [23]. It is likely that the lower vFFR gradients in the LAD are related to the greater vessel length, and subsequently greater length of the traced segment in the LAD.

A remarkable finding in the present data was the poor discriminative ability of vFFR (AUC 0.54) which forced us to refrain from proposing a binary cut-off. Instead, we divided our population into tertiles, in line with several previous studies [9,10]. A possible explanation for the poor discriminative ability in the present study might be that dichotomization of post-PCI vFFR leads to significant loss of (predictive) information. Moreover, the 5-year follow-up of the present study was significantly longer as compared to other studies on the topic (1 to 3 years) [8,9,15–18]. It could be hypothesized that the relation between post-PCI physiology and future events diminishes over time.

Finally, we observed that the median post-PCI vFFR value in our study (0.91) was comparable to the median post-PCI QFR in a post-hoc analysis of the SYNTAX II trial (0.93), but considerably lower as compared to the Hawkeye study (median post-PCI QFR 0.97) [16,17]. This could be related to study-level differences in the user-dependent selection of the distal measurement site and thus tracing length. How this impacts discriminative ability and patient outcome, and whether innovations such as implementation of artificial intelligence might eliminate any user input, should be subject of future studies.

4.1. Limitations

Several limitations of the study need to be addressed. First, the FAST Outcome study results are based on a retrospective single-center experience. Given the retrospective nature, acquisition of adequate post-PCI angiographic views was not protocol-mandated, resulting in exclusion of a significant number of potentially eligible cases (57%). Data from the recently published FAST II study indicated that proper image acquisition allows vFFR computation in over 90% of cases [24]. Secondly, information on the cause of death was unavailable in a number of patients. This could have resulted in an overestimation of the cardiovascular death and TVF rates in our study. The present findings need to be replicated in a prospective fashion to validate our conclusions (FAST III: NCT04931771). Thirdly, intravascular imaging was used in only 13.6% of patients. This might have led to higher incidences of suboptimal PCI results, and therefore worse long term patient outcomes.

5. Conclusion

A linear trend was observed between post-PCI vFFR values and the rate of TVF and TVR at 5-years follow-up. However, based on the present data, no meaningful binary cut-off value of post-PCI vFFR to predict TVF could be extracted. Post-PCI vFFR might serve a role in selecting those individuals that would benefit the most from additional post-PCI intravascular imaging or subsequent optimization.

Declaration of Competing Interest

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Appendix A. Supplementary data

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